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=> d his ful

     (FILE 'HOME' ENTERED AT 15:52:43 ON 16 OCT 2007)

     FILE 'REGISTRY' ENTERED AT 15:52:51 ON 16 OCT 2007
L1             SCR 1842
L2             STR
L3          3325 SEA SSS FUL L2 AND L1
L4             STR
L5         11336 SEA SSS FUL L4
L6             STR
L7            27 SEA SUB=L3 SSS FUL L2 AND L6
L9             STR
L10            3 SEA SUB=L5 SSS FUL L9 AND L6
               D SCAN
L11           30 SEA ABB=ON  PLU=ON  L7 OR L10

     FILE 'HCAPLUS' ENTERED AT 16:02:06 ON 16 OCT 2007
L12           14 SEA ABB=ON  PLU=ON  L11
               D STAT QUE L12
               D IBIB ABS HITSTR L12 1-14

     FILE 'REGISTRY' ENTERED AT 16:03:13 ON 16 OCT 2007
L13            STR
L14          350 SEA SSS FUL L13
L15        14630 SEA ABB=ON  PLU=ON  (L3 OR L5) NOT L11

     FILE 'HCAPLUS' ENTERED AT 16:05:23 ON 16 OCT 2007
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L18          180 SEA ABB=ON  PLU=ON  "REACTANT OR REAGENT"/RL(L)L17
L19            7 SEA ABB=ON  PLU=ON  L16 AND L18
L20            7 SEA ABB=ON  PLU=ON  L19 NOT L12
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               D IBIB ABS HITSTR L20 1-17
L21           37 SEA ABB=ON  PLU=ON  ("ST DENIS Y"/AU OR "ST DENIS YVES"/AU)
L22           32 SEA ABB=ON  PLU=ON  L21 NOT (L12 OR L20)
               D STAT QUE L22
               D IBIB ABS HITSTR L22 1-32


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   15 OCT 2007  HIGHEST RN 950725-14-1
     DICTIONARY FILE UPDATES:  15 OCT 2007  HIGHEST RN 950725-14-1

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.
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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

FILE HCAPLUS

FILE COVERS 1907 - 16 Oct 2007 VOL 147 ISS 17
FILE LAST UPDATED: 15 Oct 2007 (20071015/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 16:02:06 ON 16 OCT 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE COVERS 1907 - 16 Oct 2007 VOL 147 ISS 17
FILE LAST UPDATED: 15 Oct 2007 (20071015/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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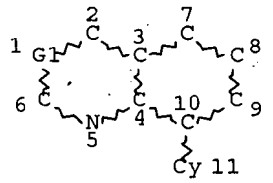
=> d stat que l12
L1 SCR 1842

L2 STR



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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
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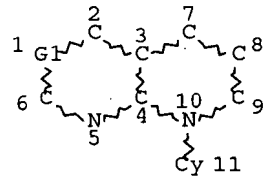
L4 STR



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STEREO ATTRIBUTES: NONE
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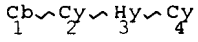
L6 STR



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STEREO ATTRIBUTES: NONE
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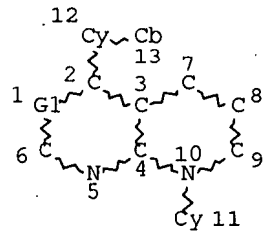

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DEFAULT MLEVEL IS ATOM
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RING(S) ARE ISOLATED OR EMBEDDED
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STEREO ATTRIBUTES: NONE
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L12 14 SEA FILE=HCAPLUS ABB=ON PLU=ON L11

=>
=>

=> d ibib abs hitstr l12 1-14

L12 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:906043 HCAPLUS Full-text
DOCUMENT NUMBER: 147:277625
TITLE: Preparation of dihydroperimidine moiety-containing bissquarylium compounds as near-infrared absorbents
INVENTOR(S): Niimi, Tatsuo; Kameyama, Kazuya; Yamano, Junzo
PATENT ASSIGNEE(S): Kyowa Hakko Chemical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 31pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007091683	A1	20070816	WO 2007-JP52386	20070209

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,

TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2006-33405 A 20060210

OTHER SOURCE(S): MARPAT 147:277625

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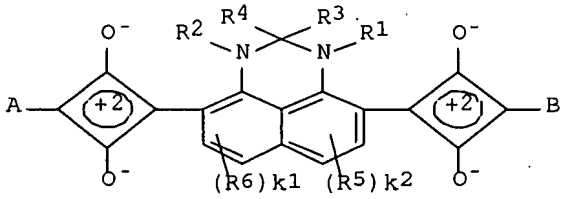

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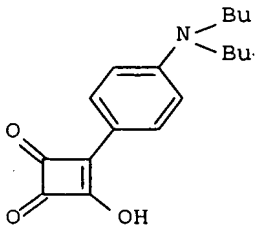


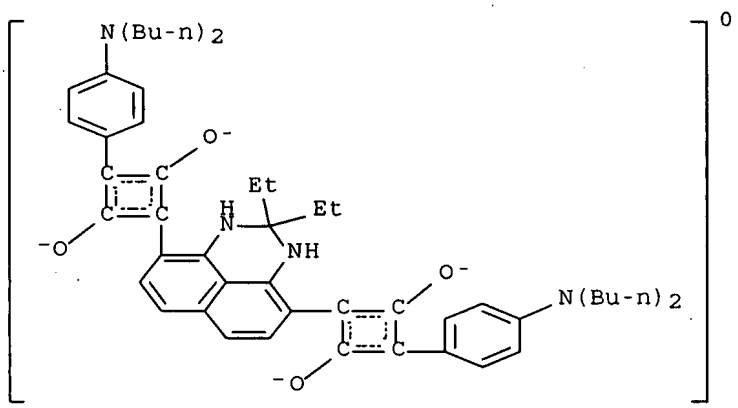
II

AB The title compds. I [R1 - R4 = H, (un)substituted alkyl, (un)substituted aralkyl, (un)substituted aryl; or R1 and R3 (or R2 and R4) together with the adjacent N-C form an (un)substituted heterocyclic ring; or R3 and R4 together with the adjacent C atom form an (un)substituted alicyclic hydrocarbon ring; k1, k2 = integer of 0 - 2; R5, R6 = halo, nitro, cyano, etc.; A, B = (un)substituted aryl, (un)substituted heterocyclic ring, G:CH-; G = (un)substituted aryl, (un)substituted heterocyclic ring] are prepared Thus, the title compound I [R1 = R2 = H; R3 = R4 = Et; k1 = k2 = 0; A = B = 4-(dibutylamino)phenyl] was prepared from reaction of 2,2-diethyl-2,3-dihydroperimidine with II. The near IR absorbing effect of compds. of this invention was demonstrated.

IT **946137-26-4P 946137-27-5P 946137-28-6P**
RL: SPN (Synthetic preparation); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(preparation of dihydroperimidine moiety-containing bissquarylium compds. as
near-IR absorbents)

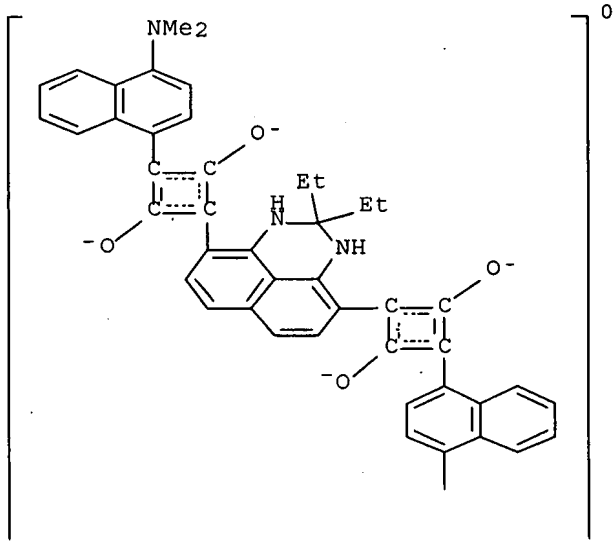
RN 946137-26-4 HCAPLUS

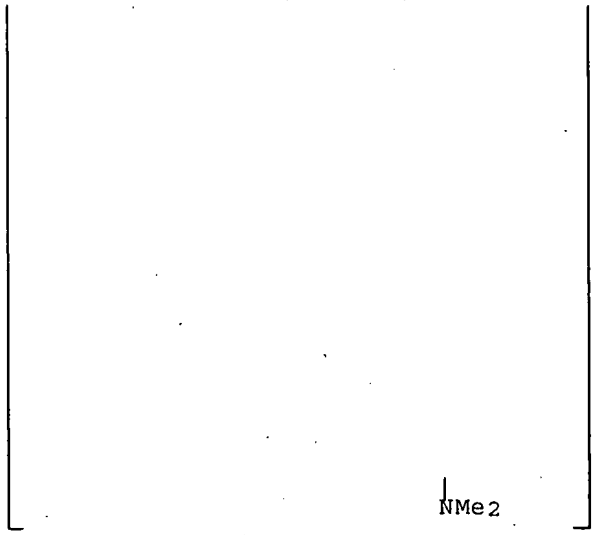
CN INDEX NAME NOT YET ASSIGNED



RN 946137-27-5 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

PAGE 1-A





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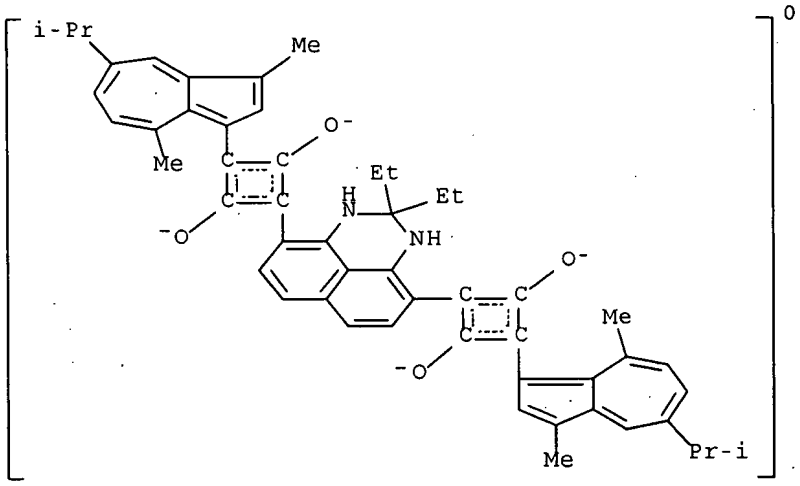
RN 946137-28-6 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1093706 HCAPLUS Full-text
DOCUMENT NUMBER: 145:438526
TITLE: Preparation of chromen-4-ones and their analogs as DNA-PK inhibitors
INVENTOR(S): Smith, Graeme Cameron Murray; Martin, Niall Morrison Barr; Cockcroft, Xiao-Ling Fan; Menear, Keith Allan; Hummersone, Marc Geoffrey; Griffin, Roger John; Frigerio, Mark; Golding, Bernard Thomas; Hardcastle, Ian Robert; Newell, David Richard; Calvert, Hilary Alan; Curtin, Nicola Jane; Desage-El Murr, Marine

PATENT ASSIGNEE(S): Kudos Pharmaceuticals Limited, UK; Cancer Research Technology Limited
SOURCE: PCT Int. Appl., 84pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006109084	A1	20061019	WO 2006-GB1379	20060413
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006264427	A1	20061123	US 2006-403606	20060413
US 2006264623	A1	20061123	US 2006-403763	20060413

PRIORITY APPLN. INFO.:

US 2005-671830P	P	20050415
US 2005-671886P	P	20050415
GB 2005-7831	A	20050418
US 2005-696064P	P	20050701
US 2005-718904P	P	20050920

OTHER SOURCE(S): MARPAT 145:438526

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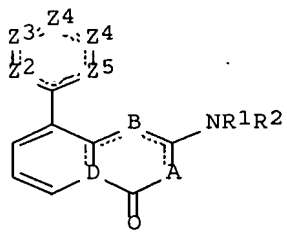

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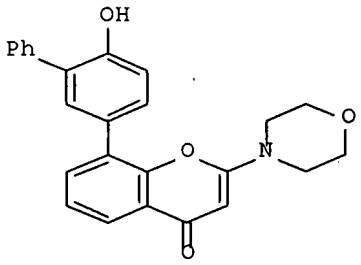


II

AB Title compds. represented by the formula I [wherein A, B and D are resp. selected from the group consisting of: (i) CH, NH, C; (ii) CH, N, N; and (iii) CH, O, C; the dotted lines represent two double bonds in the appropriate locations; and Z2-Z6 together with the carbon atom to which they are bound, form an aromatic ring; and their isomers, salts, solvates, chemical protected forms and prodrugs thereof] were prepared as DNA-PK (DNA-dependent protein kinase) inhibitors. For example, Suzuki-coupling reaction of 5-iodobiphenyl-2-ol with 2-morpholin-4-yl-8-(4,4,5,5- tetramethyl-[1,3,2]dioxaborolan-2-

yl)chromen-4-one (preparation given) provide II in 83% yield. I showed activity in DNA-PK inhibition with IC50 values of less than about 500 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of disease ameliorated by the inhibition of DNA-PK.

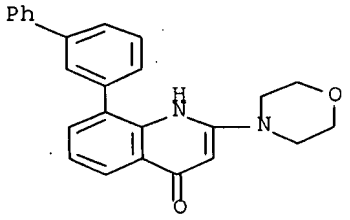
IT **912844-10-1P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of chromen-4-ones and their analogs as DNA-PK inhibitors)

RN 912844-10-1 HCAPLUS

CN 4(1H)-Quinolinone, 8-[1,1'-biphenyl]-3-yl-2-(4-morpholinyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1032101 HCAPLUS Full-text

DOCUMENT NUMBER: 145:397536

TITLE: Process for preparing pyrido[2,3-d]pyrimidin-7-one and 3,4-dihydropyrimido[4,5-d]pyrimidin-2(1h)-one derivatives

INVENTOR(S): Callahan, James Francis; Boehm, Jeffrey; Wan, Zehong; Yan, Hongxing

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 115pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

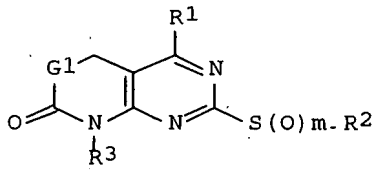
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006104917	A2	20061005	WO 2006-US10859	20060324

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2006258687 A1 20061116 US 2006-388375 20060324
PRIORITY APPLN. INFO.: US 2005-665154P P 20050325
OTHER SOURCE(S): MARPAT 145:397536
GI



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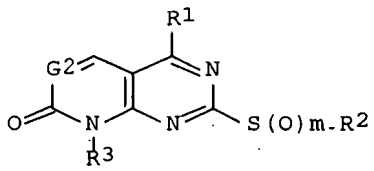
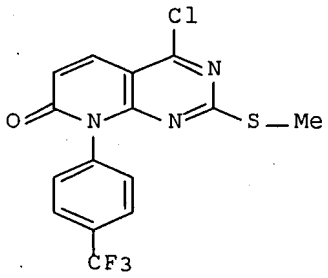


II



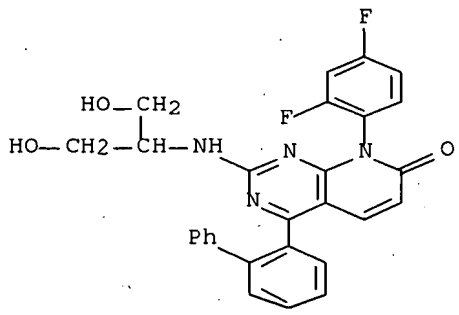
III

AB A process for the preparation of 2,4,8- trisubstituted pyrido[2,3-d]pyrimidin-7- one I or II wherein G1 is CH2 or NH; G2 is CH or N; R1 is chloro, bromo, iodo, or O-S(O)2CF3; R2 is a C1-10 alkyl; m is an integer between 0-2; R3 is a C1-10 alkyl, C3-7 cycloalkyl, C3-7 cycloalkyl C1-10 alkyl, aryl, arylC1-10 alkyl, heteroaryl, heteroarylC1-10 alkyl, heterocyclic or a heterocyclylC1-10 alkyl moiety, and wherein each of these moieties may be optionally substituted is presented. Thus, II was prepared in 70% yield from 4,6-dichloro-2-methylsulfanyl-pyrimidine-5-carboxaldehyde and 4-trifluoromethylaniline.

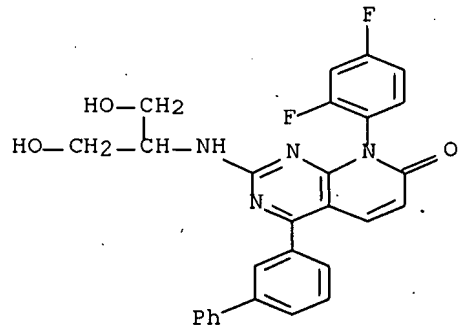
IT **911370-27-9P 911370-28-0P 911370-30-4P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparing pyrido[2,3-d]pyrimidin-7-one and 3,4-dihydropyrimido[4,5-d]pyrimidin-2(1h)-one derivs.)

RN 911370-27-9 HCAPLUS

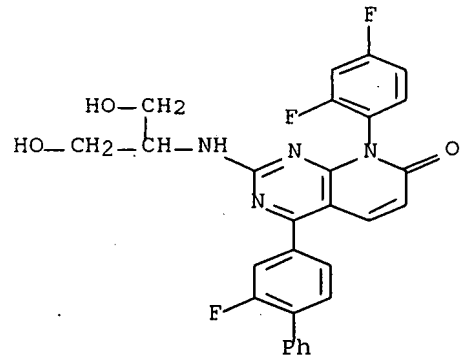
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 4-[1,1'-biphenyl]-2-yl-8-(2,4-difluorophenyl)-2-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]- (CA INDEX NAME)



RN 911370-28-0 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 4-[1,1'-biphenyl]-3-yl-8-(2,4-difluorophenyl)-2-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]- (CA INDEX NAME)



RN 911370-30-4 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,4-difluorophenyl)-4-(2-fluoro[1,1'-biphenyl]-4-yl)-2-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]- (CA INDEX NAME)



L12 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:830341 HCAPLUS Full-text
DOCUMENT NUMBER: 145:305649
TITLE: Tetrahydroisoquinolines as MCH-R1 antagonists
AUTHOR(S): Sasikumar, T. K.; Qiang, L.; Wu, W.-L.; Burnett, D. A.; Greenlee, W. J.; O'Neill, K.; Hawes, B. E.; van Heek, M.; Graziano, M.
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(18), 4917-4921
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.

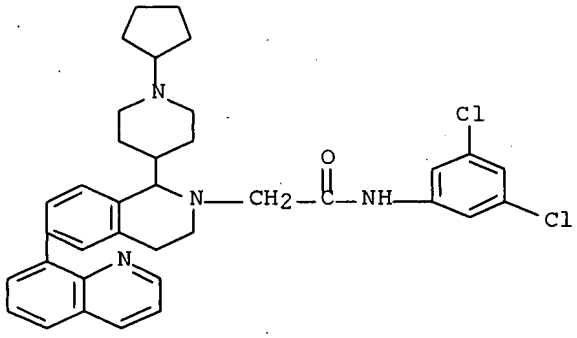
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:305649

AB A series of potent and selective inhibitors of h-MCH-R1 has been developed based on piperidine glycineamide. These structurally more rigid tetrahydroisoquinolines showed better pharmacokinetics.

IT **753029-08-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tetrahydroisoquinolines as MCH-R1 antagonists)

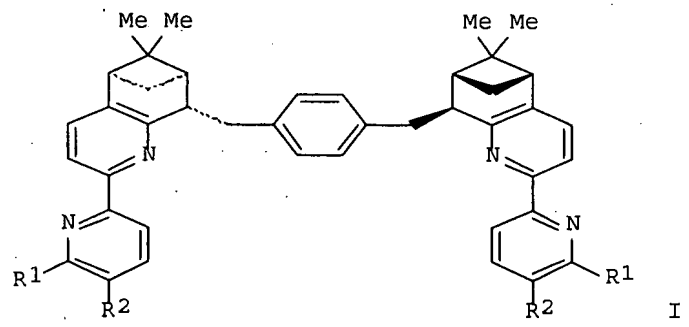
RN 753029-08-2 HCAPLUS

CN 2(1H)-Isoquinolineacetamide, 1-(1-cyclopentyl-4-piperidinyl)-N-(3,5-dichlorophenyl)-3,4-dihydro-6-(8-quinolinyl)- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1066920 HCAPLUS Full-text
DOCUMENT NUMBER: 142:231796
TITLE: Complexation behaviour of chiral tetradentate polypyridines derived from α-pinene
AUTHOR(S): Dueggeli, Mathias; Bonte, Christophe; Von Zelewsky, Alexander
CORPORATE SOURCE: Department of Chemistry, University of Fribourg, Fribourg, CH1700, Switz.
SOURCE: Inorganica Chimica Acta (2005), 358(1), 41-49
CODEN: ICHAA3; ISSN: 0020-1693
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:231796
GI



I

AB A series of ligands, where two pinene-bipyridine moieties are either connected directly, or through a p-xylene bridge were studied with respect to their complexation behavior in solution The bridged [5,6]-CHIRAGEN[p-xyl] ligands (I; (R1,R2 = H, H) II; (R1,R2 = H, p-MeOC6H4) III; (R1,R2 = Ph, H) IV; (R1,R2 = p-MeOC6H4, H)) which are substituted in 5' or 6' positions show self-assembly reactions, which lead to similar supramol. species as the unsubstituted bis-pinene-bipyridines ligands studied before. The directly connected [5,6]-CHIRAGEN[0] derivs., which are substituted at positions 5' or 6', form mononuclear silver complexes with helical chirality at the metal center.

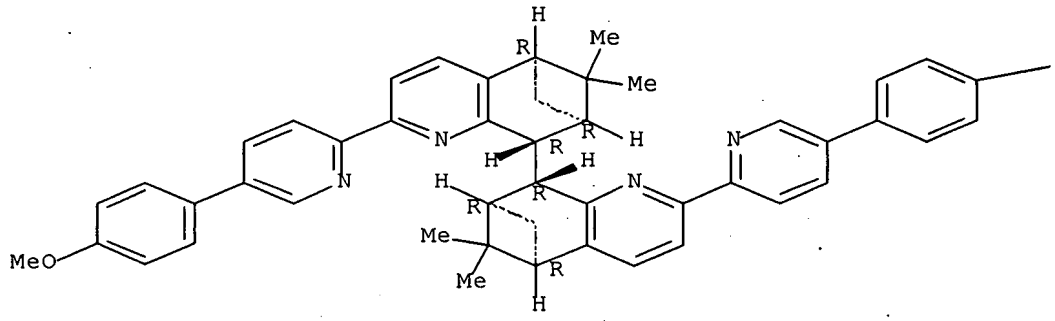
IT **608517-38-0 608517-49-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(for preparation of silver polypyridine mononuclear helical chiral complex)

RN 608517-38-0 HCAPLUS

CN 8,8'-Bi-5,7-methanoquinoline, 5,5',6,6',7,7',8,8'-octahydro-2,2'-bis[5-(4-methoxyphenyl)-2-pyridinyl]-6,6,6',6'-tetramethyl-, (5R,5'R,7R,7'R,8R,8'R)-(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

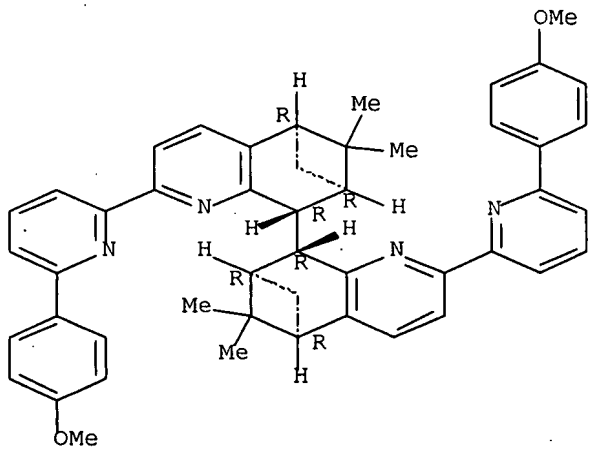
—OMe

RN 608517-49-3 HCAPLUS

CN 8,8'-Bi-5,7-methanoquinoline, 5,5',6,6',7,7',8,8'-octahydro-2,2'-bis[6-(4-

methoxyphenyl)-2-pyridinyl]-6,6,6',6'-tetramethyl-, (5R,5'R,7R,7'R,8R,8'R)-
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:739964 HCAPLUS Full-text
DOCUMENT NUMBER: 141:243353
TITLE: Preparation of diarylpiperidinyltetrahydroisoquinoline s as selective melanin concentrating hormone (MCH) receptor antagonists for the treatment of obesity and related disorders
INVENTOR(S): Sasikumar, Thavalakulamgara K.; Wu, Wen-Lian; Burnett, Duane A.; Qiang, Li
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 43 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004176355	A1	20040909	US 2004-788109	20040226
CA 2517088	A1	20040916	CA 2004-2517088	20040226
WO 2004078745	A1	20040916	WO 2004-US5780	20040226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1601664	A1	20051207	EP 2004-715072	20040226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1777596	A	20060524	CN 2004-80010904		20040226
JP 2006520399	T	20060907	JP 2006-508855		20040226
MX 2005PA09193	A	20051018	MX 2005-PA9193		20050829
PRIORITY APPLN. INFO.:			US 2003-450799P	P	20030228
			WO 2004-US5780	W	20040226

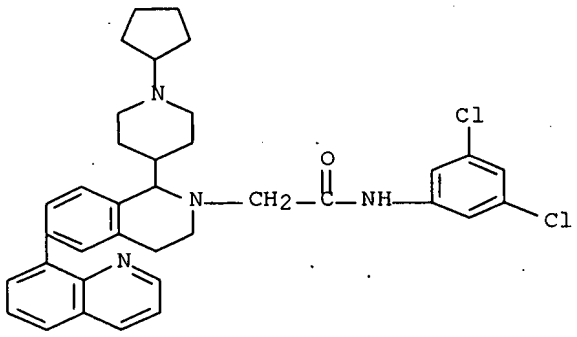
OTHER SOURCE(S): MARPAT 141:243353
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; X = CH2, SO2, CO, CHMe, CMe2; Y = (CR2R3)p, (CR2R3)pCONH, (CR2R3)pNH, CONH, CO(CR2R3)pNH, COCONH, CO(CR2R3)p; Z = (substituted) aryl, heteroaryl; m = 0, 1; n = 0, 2, 3; p = 1, 2, 3; R1 = H, acyl, alkyl, cycloalkyl, cycloalkylalkyl, etc.; R2, R3 = H, alkoxy, alkyl; R2R3 = atoms to form a 3-7 membered ring; R4 = (substituted) aryl, heteroaryl; YR4 = (substituted) benzimidazol-2-ylmethyl; with provisos], were prepared Thus, title compound (II) antagonized MCH with Ki = 6.4 nM.

IT **753029-08-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diarylpiperidinyltetrahydroisoquinolines as selective melanin concentrating hormone receptor antagonists for the treatment of obesity and related disorders)

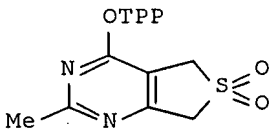
RN 753029-08-2 HCAPLUS
CN 2(1H)-Isoquinolineacetamide, 1-(1-cyclopentyl-4-piperidinyl)-N-(3,5-dichlorophenyl)-3,4-dihydro-6-(8-quinolinyl)- (CA INDEX NAME)



L12 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2003:746732 HCAPLUS Full-text
DOCUMENT NUMBER:	140:4889
TITLE:	Novel porphyrin-quinazoline conjugates via the Diels-Alder reaction
AUTHOR(S):	Tome, Joao P. C.; Tome, Augusto C.; Neves, Maria G. P. M. S.; Almeida Paz, Filipe A.; Gates, Paul J.; Klinowski, Jacek; Cavaleiro, Jose A. S.
CORPORATE SOURCE:	Department of Chemistry, University of Aveiro, Aveiro,

3810-193, Port.
SOURCE: Tetrahedron (2003), 59(40), 7907-7913
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:4889
GI



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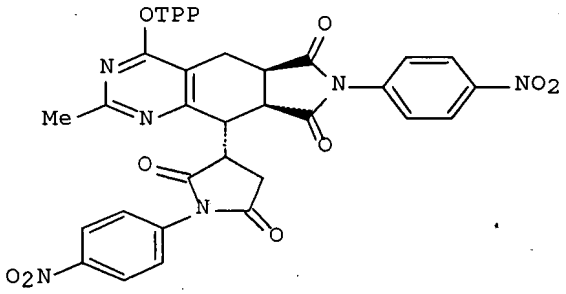


II

AB Novel derivs. of meso-tetraphenylporphyrin with appended quinazoline moieties were synthesized, via the Diels-Alder reaction, between a 4-(porphyrinyl)pyrimidine ortho-quinodimethane I and 1,4-benzoquinone, 1,4-naphthoquinone and N-(p-nitrophenyl)maleimide. The structure of one bis adduct, II, was established by X-ray crystallog. and mass spectrometry. We have unequivocally confirmed that the 2:1 adducts obtained from the reaction of pyrimidine-fused 3-sulfolenes with N-arylmaleimides have an open-chain structure and not a cyclooctapyrimidine structure, as previously published.

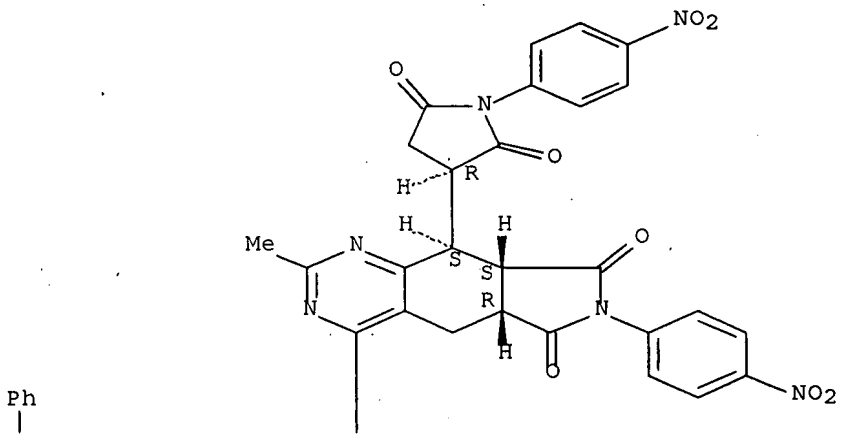
IT **627466-38-0P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (generation and Diels-Alder reaction of 4-(porphyrinyl)pyrimidine ortho-quinodimethane and proof of product open-chain structure by x-ray anal. of bis-adduct)

RN 627466-38-0 HCAPLUS

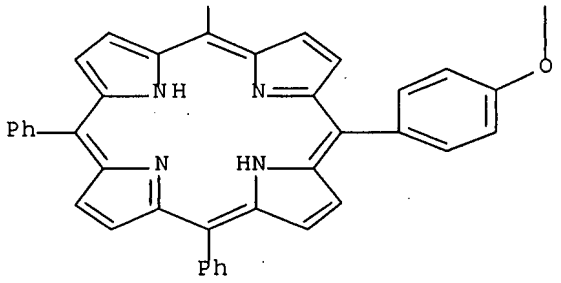
CN 5H-Pyrrolo[3,4-g]quinazoline-6,8(5aH,7H)-dione, 8a,9-dihydro-2-methyl-7-(4-nitrophenyl)-9-[(3R)-1-(4-nitrophenyl)-2,5-dioxo-3-pyrrolidinyl]-4-[4-(10,15,20-triphenyl-21H,23H-porphin-5-yl)phenoxy]-, (5aR,8aS,9S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



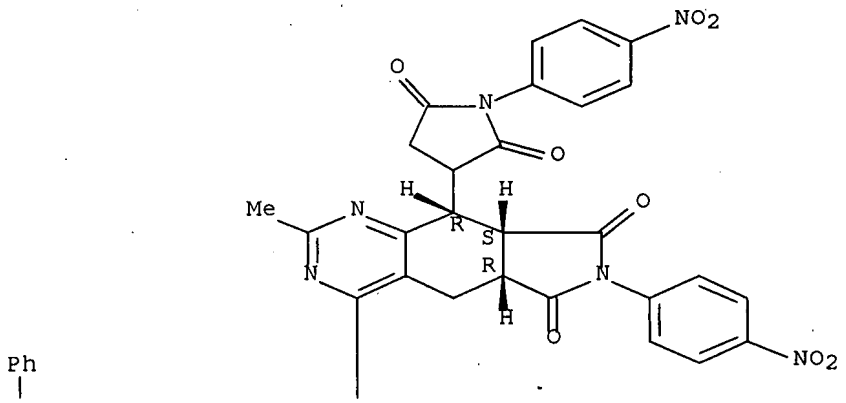
PAGE 2-A



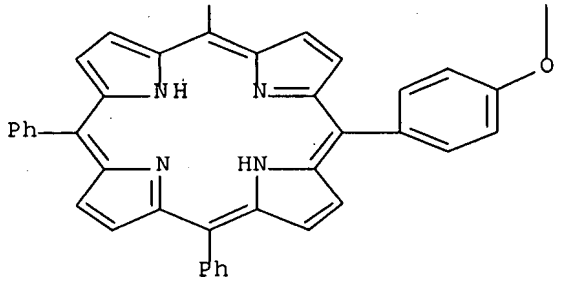
IT **627466-40-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(generation and Diels-Alder reaction of 4-(porphyrinyl)pyrimidine ortho-quinodimethane and proof of product open-chain structure by x-ray anal. of bis-adduct)
RN 627466-40-4 HCAPLUS
CN 5H-Pyrrolo[3,4-g]quinazoline-6,8(5aH,7H)-dione, 8a,9-dihydro-2-methyl-7-(4-nitrophenyl)-9-[1-(4-nitrophenyl)-2,5-dioxo-3-pyrrolidinyl]-4-[4-(10,15,20-triphenyl-21H,23H-porphin-5-yl)phenoxy]-, (5aR,8aS,9R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

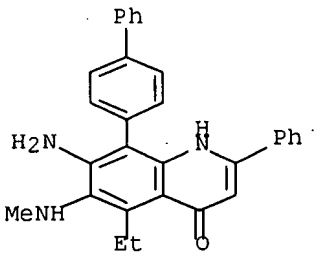
L12 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:556622 HCAPLUS Full-text
DOCUMENT NUMBER: 140:104333
TITLE: Virtual screening and rational drug design method using structure generation system based on 3D-QSAR and docking
AUTHOR(S): Chen, H. F.; Dong, X. C.; Zen, B. S.; Gao, K.; Yuan, S. G.; Panaye, A.; Doucet, J.-P.; Fan, B. T.
CORPORATE SOURCE: ITODYS, CNRS UMR7086, Universite Paris 7-Denis Diderot, Paris, 75005, Fr.
SOURCE: SAR and QSAR in Environmental Research (2003), 14(4), 251-264
CODEN: SQERED; ISSN: 1062-936X
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An efficient virtual and rational drug design method is presented. It combines virtual bioactive compound generation with 3D-QSAR model and docking. Using this method, it is possible to generate a lot of highly diverse mols. and find virtual active lead compds. The method was validated by the study of a set of anti-tumor drugs. With the constraints of pharmacophore obtained by DISCO implemented in SYBYL 6.8, 97 virtual bioactive compds. were generated, and their anti-tumor activities were predicted by CoMFA. Eight structures with high activity were selected and screened by the 3D-QSAR model. The most active generated structure was further investigated by modifying its structure in order to increase the activity. A comparative docking study with telomeric receptor was carried out, and the results showed that the generated structures could form more stable complexes with receptor than the reference compound selected from exptl. data. This investigation showed that the proposed method was a feasible way for rational drug design with high screening efficiency.

IT **646508-25-0**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(virtual screening and rational drug design method using structure generation system based on 3D-QSAR and docking)

RN 646508-25-0 HCAPLUS

CN 4(1H)-Quinolinone, 7-amino-8-[1,1'-biphenyl]-4-yl-5-ethyl-6-(methylamino)-2-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:491962 HCAPLUS Full-text

DOCUMENT NUMBER: 139:292126

TITLE: Synthetic routes for a new family of chiral tetradentate ligands containing pyridine rings

AUTHOR(S): Dueggeli, Mathias; Goujon-Ginglinger, Catherine; Ducotterd, Sarah Richard; Mauron, David; Bonte, Christophe; von Zelewsky, Alexander; Stoeckli-Evans, Helen; Neels, Antonia

CORPORATE SOURCE: Department of Chemistry, University of Fribourg, Perolles, Switz.

SOURCE: Organic & Biomolecular Chemistry (2003), 1(11), 1894-1899
CODEN: OBCRAK; ISSN: 1477-0520

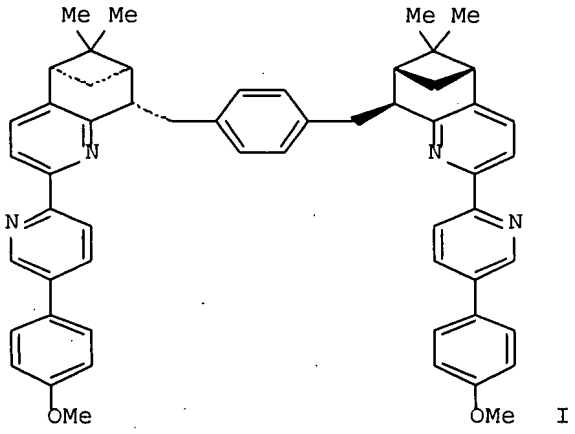
PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:292126

GI



I

AB A series of new tetradentate ligands, e.g. I, containing two bipyridine groups or two pyridine moieties carrying amine substituents has been synthesized either from 5'- and 6'-substituted chiral bipyridines, or from chiral pyridine derivs. These precursors have been prepared from (-)-α-pinene or (-)-myrtenal, resp. The structures of three tetradentate-, and of five chiral bipyridine ligands have been determined by x-ray diffraction.

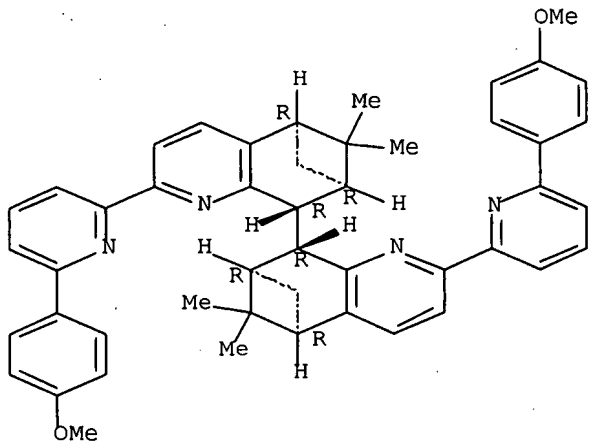
IT **608517-49-3P**

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (crystal structure; synthesis of a new family of chiral tetradentate ligands containing pyridine rings)

RN 608517-49-3 HCAPLUS

CN 8,8'-Bi-5,7-methanoquinoline, 5,5',6,6',7,7',8,8'-octahydro-2,2'-bis[6-(4-methoxyphenyl)-2-pyridinyl]-6,6,6',6'-tetramethyl-, (5R,5'R,7R,7'R,8R,8'R)- (CA INDEX NAME)

Absolute stereochemistry.



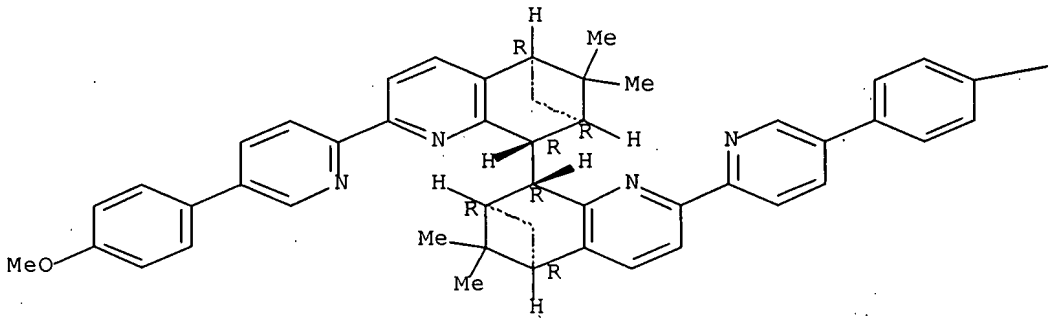
IT **608517-38-0P 608517-48-2P**

RL: SPN (Synthetic preparation); PREP (Preparation) (synthesis of a new family of chiral tetradentate ligands containing

pyridine rings)
RN 608517-38-0 HCAPLUS
CN 8,8'-Bi-5,7-methanoquinoline, 5,5',6,6',7,7',8,8'-octahydro-2,2'-bis[5-(4-methoxyphenyl)-2-pyridinyl]-6,6,6',6'-tetramethyl-, (5R,5'R,7R,7'R,8R,8'R)-(CA INDEX NAME)

Absolute stereochemistry.

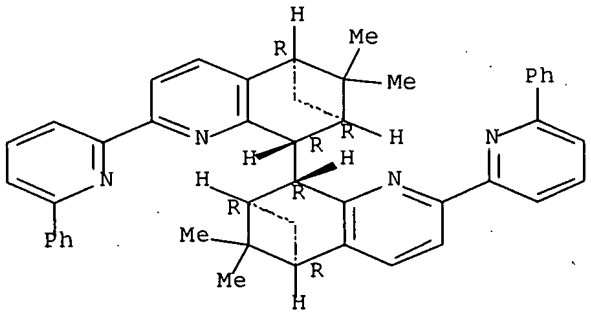
PAGE 1-A



PAGE 1-B

RN 608517-48-2 HCAPLUS
CN 8,8'-Bi-5,7-methanoquinoline, 5,5',6,6',7,7',8,8'-octahydro-6,6,6',6'-tetramethyl-2,2'-bis(6-phenyl-2-pyridinyl)-, (5R,5'R,7R,7'R,8R,8'R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

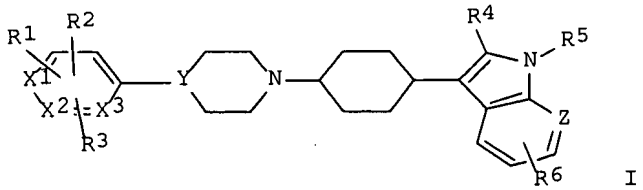
L12 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:809092 HCAPLUS Full-text
DOCUMENT NUMBER: 135:344505
TITLE: Preparation of arylpiperazinyl-cyclohexyl indole derivatives for the treatment of depression

INVENTOR(S): Mewshaw, Richard E.; Zhou, Ping; Zhou, Dahui; Meagher, Kristin L.; Asselin, Magda; Evrard, Deborah A.; Gilbert, Adam M.
PATENT ASSIGNEE(S): American Home Products Corp, USA
SOURCE: U.S., 62 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6313126	B1	20011106	US 1999-476254	19991230
US 2002045628	A1	20020418	US 2001-969910	20011003
US 6465482	B2	20021015		

PRIORITY APPLN. INFO.: US 1999-155199P P 19990107
US 1999-476254 A3 19991230

OTHER SOURCE(S): MARPAT 135:344505
GI



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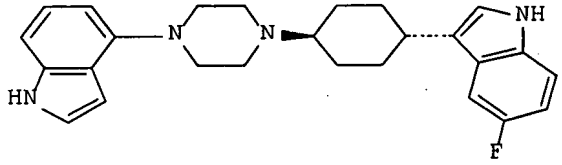


II

AB Arylpiperazinyl-cyclohexyl indole derivs. of formula I [R1-R3 = H, halo, CF3, alkyl, alkoxy, MeSO2, or together can form a 5-7 membered carbocyclic or heterocyclic ring; R4 = H, halo, alkyl; R5 = H, alkyl, alkylaryl, aryl; R6 = H, halo, CF3, CN, carbamido, alkoxy; X1-X3, Y, Z = C, N] are prepared which are useful for the treatment of serotonin-affected neurol. disorders such as depression and anxiety. Thus, II was prepared from 4-(5-fluoro-1H-indol-3-yl)cyclohexanone and 1-(indol-4-yl)piperazine, and was shown to be active towards 5-HT1A receptors with Ki = 4.62 nM.

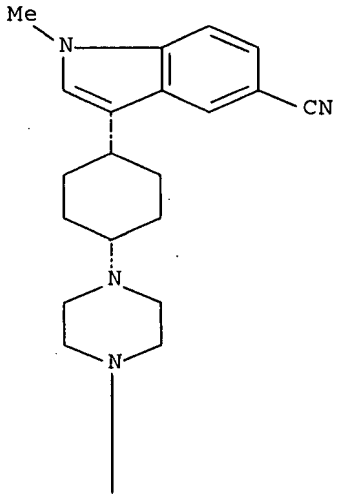
IT **282546-03-6P 282546-05-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylpiperazinyl-cyclohexyl indole derivs. for treatment of depression)

RN 282546-03-6 HCAPLUS

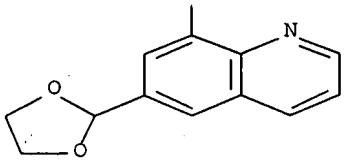
CN 1H-Indole-5-carbonitrile, 3-[cis-4-[4-[6-(1,3-dioxolan-2-yl)-8-quinolinyl]-1-piperazinyl]cyclohexyl]-1-methyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



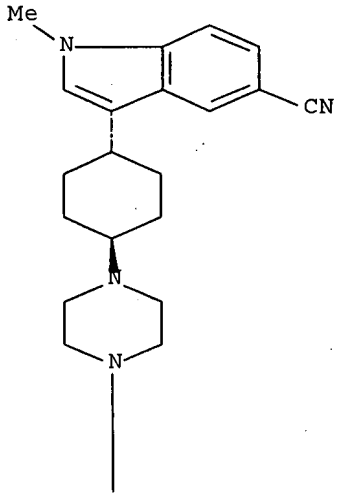
PAGE 2-A



RN 282546-05-8 HCAPLUS
CN 1H-Indole-5-carbonitrile, 3-[trans-4-[4-[6-(1,3-dioxolan-2-yl)-8-quinolinyl]-1-piperazinyl]cyclohexyl]-1-methyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



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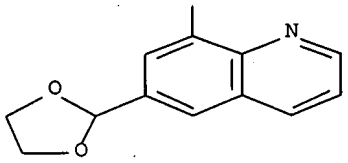


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:475638 HCAPLUS Full-text
DOCUMENT NUMBER: 133:105051
TITLE: Preparation of arylpiperazinyl-cyclohexyl indoles for the treatment of depression
INVENTOR(S): Mewshaw, Richard Eric; Zhou, Ping; Zhou, Dahui; Meagher, Kristin Lynne; Asselin, Magda; Evrard, Deborah Ann; Gilbert, Adam Matthew
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 182 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

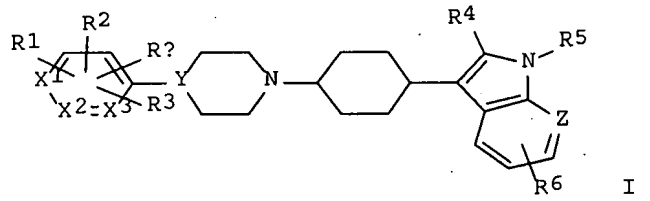
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040554	A1	20000713	WO 2000-US223	20000106

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

	MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2355342		A1	20000713	CA 2000-2355342	20000106
BR 2000007424		A	20011009	BR 2000-7424	20000106
EP 1147083		A1	20011024	EP 2000-903114	20000106
EP 1147083		B1	20040616		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
HU 2002000309		A2	20020629	HU 2002-309	20000106
JP 2002534411		T	20021015	JP 2000-592263	20000106
AT 269303		T	20040715	AT 2000-903114	20000106
PT 1147083		T	20040930	PT 2000-903114	20000106
ES 2219302		T3	20041201	ES 2000-903114	20000106
ZA 2001005190		A	20020923	ZA 2001-5190	20010622
MX 2001PA06853		A	20011001	MX 2001-PA6853	20010704
NO 2001003369		A	20010903	NO 2001-3369	20010706
PRIORITY APPLN. INFO.:				US 1999-226583	A 19990107
				WO 2000-US223	W 20000106

OTHER SOURCE(S): MARPAT 133:105051

GI



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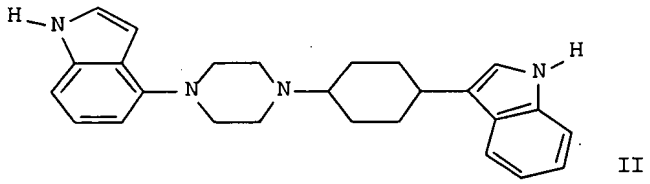


II

AB The title compds. [I; Ra, R1-R3 = H, halo, CF3, etc.; two adjacent of Ra and R1-3 together can form (un)substituted 5-7 membered carbocyclic or heterocyclic ring; R4 = H, halo, alkyl; R5 = H, alkyl, arylalkyl, aryl; R6 = H, halo, CF3, etc.; X1-X3 = each C or one of X1-X3 may be N; Y = CH, N; Z = C, N] and their pharmaceutically acceptable salts, useful for the treatment of serotonin-affected neurol. disorders, were prepared E.g., a multi-step synthesis of cis-II and trans-II which showed Ki of 32.0 nM and 5.29 nM against 5-HT1A binding, resp., was given.

IT **282546-03-6P 282546-05-8P**

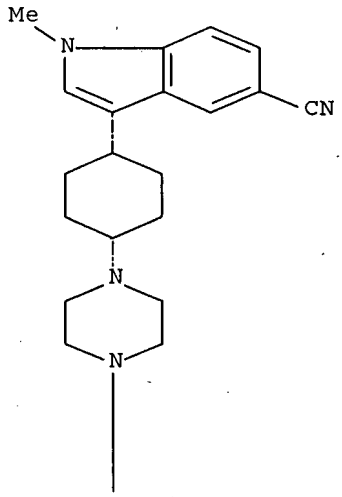
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT

(Reactant or reagent); USES (Uses)
(preparation of arylpiperazinyl-cyclohexyl indoles for the treatment of depression)

RN 282546-03-6 HCAPLUS
CN 1H-Indole-5-carbonitrile, 3-[cis-4-[4-[6-(1,3-dioxolan-2-yl)-8-quinolinyl]-1-piperazinyl]cyclohexyl]-1-methyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



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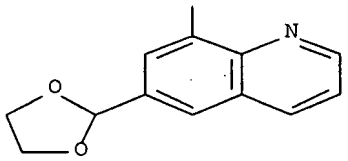
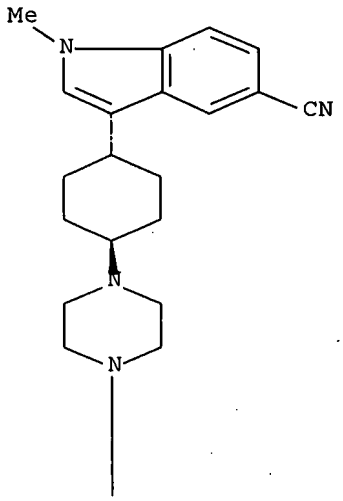


RN 282546-05-8 HCAPLUS
CN 1H-Indole-5-carbonitrile, 3-[trans-4-[4-[6-(1,3-dioxolan-2-yl)-8-quinolinyl]-1-piperazinyl]cyclohexyl]-1-methyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



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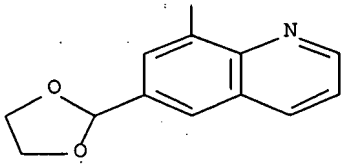


IT **282546-04-7P 282546-06-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylpiperazinyl-cyclohexyl indoles for the treatment of depression)

RN 282546-04-7 HCAPLUS

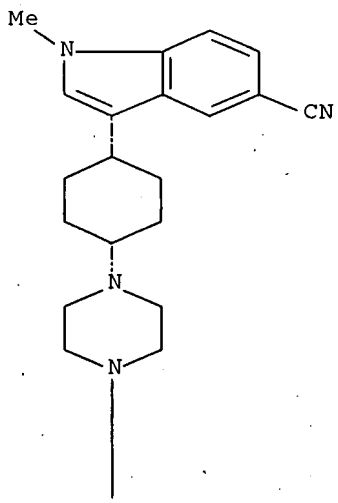
CN 1H-Indole-5-carbonitrile, 3-[cis-4-[4-[6-(1,3-dioxolan-2-yl)-8-quinolinyl]-1-piperazinyl]cyclohexyl]-1-methyl-, ethanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 282546-03-6
CMF C32 H35 N5 O2

Relative stereochemistry.

PAGE 1-A



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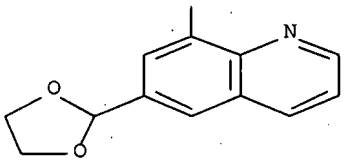
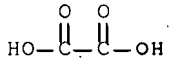


CM 2

CRN 144-62-7
CMF C2 H2 O4



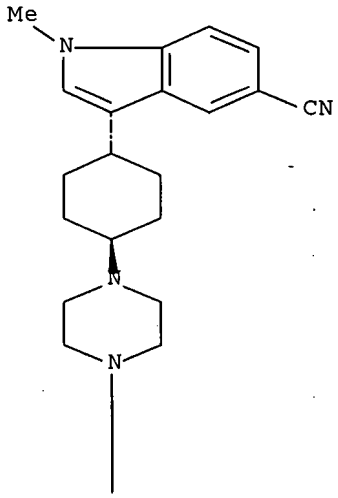
RN 282546-06-9 HCAPLUS
CN 1H-Indole-5-carbonitrile, 3-[trans-4-[4-[6-(1,3-dioxolan-2-yl)-8-quinolinyl]-1-piperazinyl]cyclohexyl]-1-methyl-, ethanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 282546-05-8
CMF C32 H35 N5 O2

Relative stereochemistry.

PAGE 1-A



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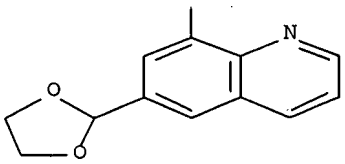
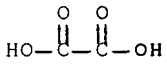


CM 2

CRN 144-62-7
CMF C2 H2 O4



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:189938 HCAPLUS Full-text
DOCUMENT NUMBER: 126:186111
TITLE: Preparation of heterocyclic carboxylic acid derivatives as retinoid receptor agonists
INVENTOR(S): Kikuchi, Kouichi; Tagami, Katsuya; Yoshimura, Hiroyuki; Hibi, Shigeki; Nagai, Mitsuo; Abe, Shinya; Okita, Makoto; Hida, Takayuki; Higashi, Seiko; Tokuhara, Naoki; Kobayashi, Seiichi; et al.
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9702244	A1	19970123	WO 1996-JP1782	19960627
W: AU, CA, CN, HU, KR, MX, NO, NZ, RU, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 09071566	A	19970318	JP 1996-141433	19960604
JP 3964478	B2	20070822		
AU 9662422	A	19970205	AU 1996-62422	19960627
EP 838453	A1	19980429	EP 1996-921104	19960627
EP 838453	B1	20050427		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
AT 294160	T	20050515	AT 1996-921104	19960627
EP 1559709	A1	20050803	EP 2005-1823	19960627
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
US 5977108	A	19991102	US 1997-981770	19971230
US 6329402	B1	20011211	US 1999-313087	19990517
US 2002032202	A1	20020314	US 2001-910012	20010723
US 6541474	B2	20030401		
US 2002103234	A1	20020801	US 2001-910068	20010723
US 6630463	B2	20031007		
US 2003144276	A1	20030731	US 2003-336756	20030106
US 6884808	B2	20050426		

PRIORITY APPLN. INFO.:

JP 1995-166004	A	19950630
JP 1996-141433	A	19960604
EP 1996-921104	A3	19960627
WO 1996-JP1782	W	19960627
US 1997-981770	A3	19971230
US 1999-313087	XX	19990517
US 2001-910068	A3	20010723

OTHER SOURCE(S): MARPAT 126:186111
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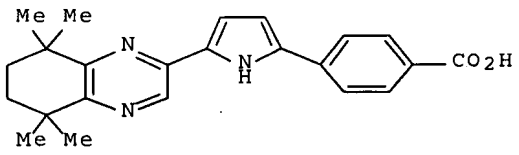


I

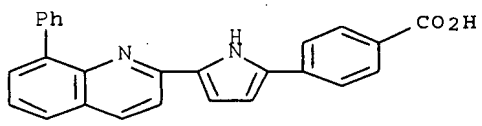
AB Heterocyclic carboxylic acid derivs. AB(D)nCOM [A is a heteroaryl group which has at least one nitrogen atom and may be substituted, or the like; B is heteroarylene, CONH, CR6:CR7 (R6 and R7 being each H, lower alkyl or the like) or the like; D is arylene, heteroarylene or the like; n is 0 or 1; and M is hydroxyl, lower alkoxy or the like] are prepared In an in vitro retinoid receptor binding assay, tetrahydroquinoxaline derivative I showed IC50 of 1.6 nM, vs. IC50 of 1.1 nM shown by all-trans-retinoic acid.

IT **187401-02-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic carboxylic acid derivs. as retinoid receptor agonists)

RN 187401-02-1 HCAPLUS

CN Benzoic acid, 4-[5-(8-phenyl-2-quinolinyl)-1H-pyrrol-2-yl]- (9CI) (CA INDEX NAME)



L12 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:408613 HCAPLUS Full-text

DOCUMENT NUMBER: 115:8613

TITLE: Reaction of aromatic N-oxides with dipolarophiles. XV. Formation of the 1,5-sigmatropy products and their double ene reaction products

AUTHOR(S): Matsuoka, Toshikazu; Ono, Kikuma; Harano, Kazunobu; Hisano, Takuzo

CORPORATE SOURCE: Fac. Pharm. Sci., Kumamoto Univ., Kumamoto, 862, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (1991), 39(1), 10-17
CODEN: CPBTAL; ISSN: 0009-2363

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 115:8613

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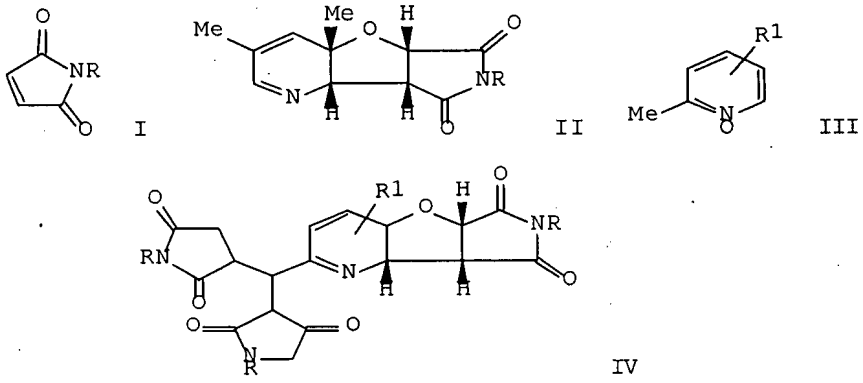


I II III IV

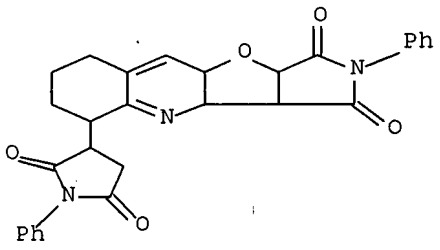
AB The pericyclic reaction of 3,5-dimethylpyridine N-oxide with maleimides I (R = Bu, Ph, substituted Ph) gave furopyridine cycloadducts II formed by the 1,5-sigmatropic rearrangement of the primary exo-cycloadducts. The mol. structure

of II (R = Bu) was determined the by the x-ray crystallog. method. In the reaction of 2-alkylpyridine N-oxides III (R1 = 3-, 5-Me, 5-Et) with N-substituted maleimides, a series of 1:3 ene reaction products of the type IV (R = Ph, substituted Ph, Bu) were obtained. The primary exo-cycloadducts readily transform into the endo-1,5-sigmatropic rearrangement products, which again react with two mols. of N-substituted maleimide to give the 1:3 ene reaction products. The observed reaction behavior and plausible reaction pathways are discussed in terms of frontier MO considerations.

IT **134220-57-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 134220-57-8 HCAPLUS

CN 1H-Pyrrolo[3',4':4,5]furo[3,2-b]quinoline-1,3(2H)-dione, 9-(2,5-dioxo-1-phenyl-3-pyrrolidinyl)-3a,4a,6,7,8,9,10a,10b-octahydro-2-phenyl- (9CI) (CA INDEX NAME)



L12 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:30599 HCAPLUS Full-text

DOCUMENT NUMBER: 94:30599

TITLE: Reaction of N-phenylmaleimide with 2- and 4-vinylpyridines

AUTHOR(S): Terent'ev, P. B.; Kartsev, V. G.; Kost, A. N.

CORPORATE SOURCE: Mosk. Gos. Univ., Moscow, USSR

SOURCE: Khimiya Geterotsiklicheskikh Soedinenii (1980), (8), 1075-8
CODEN: KGSSAQ; ISSN: 0453-8234

DOCUMENT TYPE: Journal

LANGUAGE: Russian

OTHER SOURCE(S): CASREACT 94:30599

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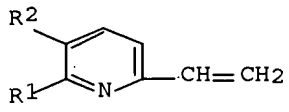

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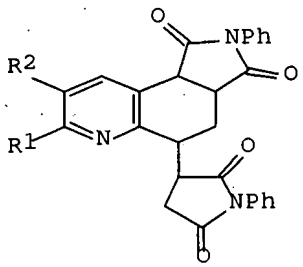

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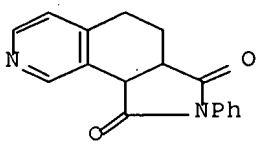
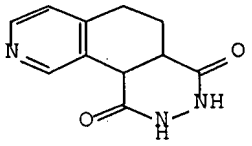


III



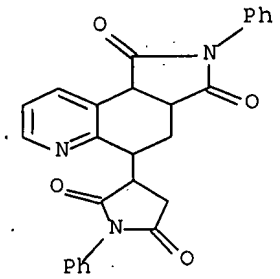
IV

AB Reaction of vinylpyridines I (R1 = R2 = H; R1 = Me, R2 = H; R1 = H, R2 = Me, Et) with N-phenylmaleimide gave 25-37% bisadducts II. The same reaction with 4-vinylpyridine gave the monoadduct III, which gave 97% pyridazoisoquinoline IV when treated with N2H4, H2O. Spectral data for II were tabulated.

IT **76071-69-7P 76071-70-0P 76071-71-1P 76071-72-2P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and spectra of)

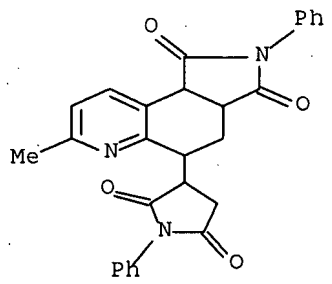
RN 76071-69-7 HCAPLUS

CN 1H-Pyrrolo[3,4-f]quinoline-1,3(2H)-dione, 5-(2,5-dioxo-1-phenyl-3-pyrrolidinyl)-3a,4,5,9b-tetrahydro-2-phenyl- (9CI) (CA INDEX NAME)

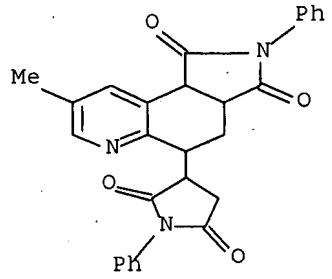


RN 76071-70-0 HCAPLUS

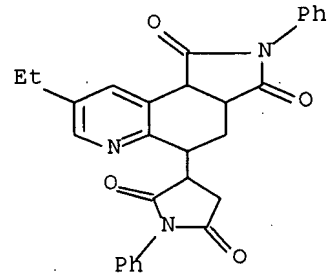
CN 1H-Pyrrolo[3,4-f]quinoline-1,3(2H)-dione, 5-(2,5-dioxo-1-phenyl-3-pyrrolidinyl)-3a,4,5,9b-tetrahydro-7-methyl-2-phenyl- (9CI) (CA INDEX NAME)



RN 76071-71-1 HCAPLUS
CN 1H-Pyrrolo[3,4-f]quinoline-1,3(2H)-dione, 5-(2,5-dioxo-1-phenyl-3-pyrrolidinyl)-3a,4,5,6b-tetrahydro-8-methyl-2-phenyl- (9CI) (CA INDEX NAME)



RN 76071-72-2 HCAPLUS
CN 1H-Pyrrolo[3,4-f]quinoline-1,3(2H)-dione, 5-(2,5-dioxo-1-phenyl-3-pyrrolidinyl)-8-ethyl-3a,4,5,9b-tetrahydro-2-phenyl- (9CI) (CA INDEX NAME)



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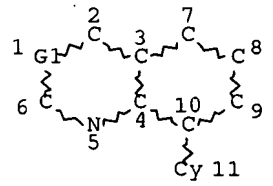
L1 SCR 1842
L2 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
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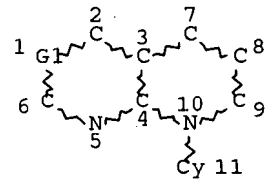
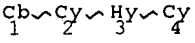
L4 STR



VAR G1=C/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

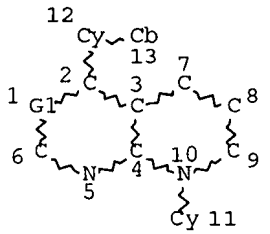
STEREO ATTRIBUTES: NONE
L5 11336 SEA FILE=REGISTRY SSS FUL L4
L6 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS MCY AT 2
GGCAT IS PCY AT 3
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 4

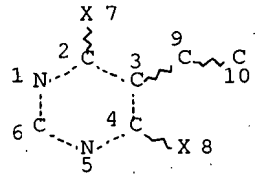
STEREO ATTRIBUTES: NONE
L7 27 SEA FILE=REGISTRY SUB=L3 SSS FUL L2 AND L6
L9 STR



VAR G1=C/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE
L10 3 SEA FILE=REGISTRY SUB=L5 SSS FUL L9 AND L6
L11 30 SEA FILE=REGISTRY ABB=ON PLU=ON L7 OR L10
L12 14 SEA FILE=HCAPLUS ABB=ON PLU=ON L11
L13 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE
L14 350 SEA FILE=REGISTRY SSS FUL L13
L15 14630 SEA FILE=REGISTRY ABB=ON PLU=ON (L3 OR L5) NOT L11
L16 1416 SEA FILE=HCAPLUS ABB=ON PLU=ON L15/P
L17 252 SEA FILE=HCAPLUS ABB=ON PLU=ON L14
L18 180 SEA FILE=HCAPLUS ABB=ON PLU=ON "REACTANT OR REAGENT"/RL(L)L17

L19 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 AND L18
L20 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 NOT L12

=>

=>

=> d ibib abs hitstr l20 1-17

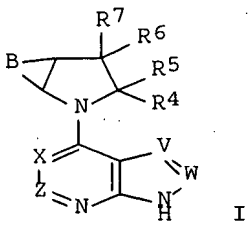
L20 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:888369 HCAPLUS Full-text
DOCUMENT NUMBER: 145:293091
TITLE: Preparation of bicyclic heteroaromatic derivatives as anticancer agents
INVENTOR(S): Kauffman, Goss Stryker; Li, Chao; Lippa, Blaise Scott; Morris, Joel; Pan, Gonghua
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 152pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006090261	A1	20060831	WO 2006-IB406	20060215

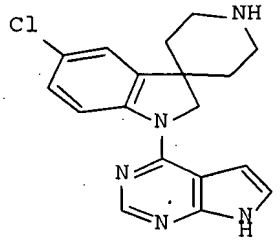
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-656467P P 20050224
OTHER SOURCE(S): MARPAT 145:293091
GI



I



II

AB The title compds. I [X, Z, V and W = N or CR1 (R1 = H, halo, CN, etc.); R4 = H, alkyl, (CR11R12)t(aryl), (CR11R12)t(4-10 membered heterocyclyl); R5 = H, alkyl, or R4 and R5 are taken together to form an oxo moiety; R6 and R7 are taken together to form a 4-10 membered (bi)cyclic or hetero(bi)cyclic ring system; B represents a fused 5-6 membered aromatic ring containing 0-2

heteroatoms; with provisos], useful for treating abnormal cell growth in mammals (no specific data given), were prepared Thus, reacting 4-chloro-7H-pyrrolo[2,3-d]pyrimidine with tert-Bu 5-chloro-1,2-dihydro-1'H- spiro[indole-3,4'-piperidine]-1'-carboxylate followed by deprotection afforded II. The invention also relates to methods of treating abnormal cell growth in mammals by administering the compds. I and to pharmaceutical compns. for treating such disorders which contain the compds. I.

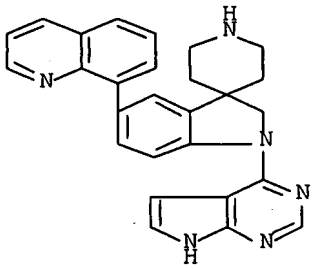
IT **908281-82-3P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of bicyclic heteroarom. derivs. as anticancer agents)

RN 908281-82-3 HCAPLUS

CN Spiro[3H-indole-3,4'-piperidine], 1,2-dihydro-1-(1H-pyrrolo[2,3-d]pyrimidin-4-yl)-5-(8-quinolinyl)- (9CI) (CA INDEX NAME)



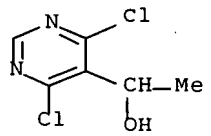
IT **60025-05-0P**, 1-(4,6-Dichloropyrimidin-5-yl)ethanol
60025-06-1P, 1-(4,6-Dichloropyrimidin-5-yl)ethanone

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**

(preparation of bicyclic heteroarom. derivs. as anticancer agents)

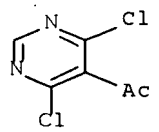
RN 60025-05-0 HCAPLUS

CN 5-Pyrimidinemethanol, 4,6-dichloro-α-methyl- (9CI) (CA INDEX NAME)



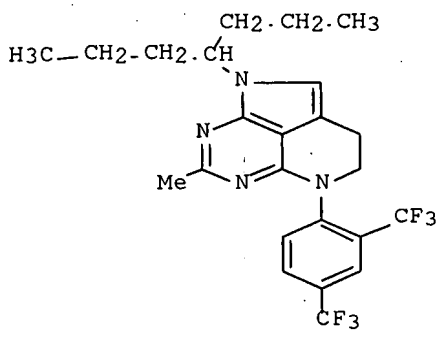
RN 60025-06-1 HCAPLUS

CN Ethanone, 1-(4,6-dichloro-5-pyrimidinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

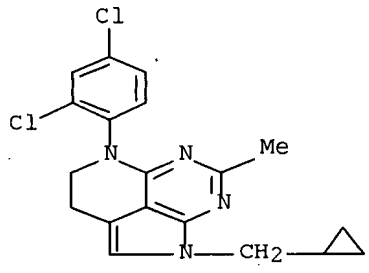
L20 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:636161 HCAPLUS Full-text
DOCUMENT NUMBER: 143:221826
TITLE: Substituted tetraazaacenaphthylenes as potent CRF1 receptor antagonists for the treatment of depression and anxiety
AUTHOR(S): St-Denis, Y.; Di Fabio, R.; Bernasconi, G.; Castiglioni, E.; Contini, S.; Donati, D.; Fazzolari, E.; Gentile, G.; Ghirlanda, D.; Marchionni, C.; Messina, F.; Micheli, F.; Pavone, F.; Pasquarello, A.; Sabbatini, F. M.; Zampori, M. G.; Arban, R.; Vitulli, G.
CORPORATE SOURCE: Department of Medicinal Chemistry, GlaxoSmithKline Medicines Research Center, Verona, 37135, Italy
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(16), 3713-3716
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:221826
GI



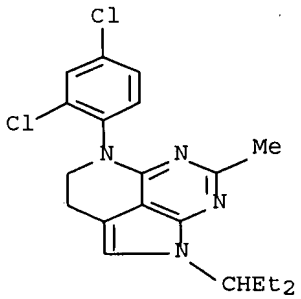
I

AB Two isomers of the hexahydro-tetraazaacenaphthylene templates are presented as novel, potent, and selective corticotropin releasing factor-1 (CRF1) receptor antagonists. In this paper, the authors report the affinity and SAR of a series of compds., as well as pharmacokinetic characterization of a chosen set. The anxiolytic activity of a selected example (I) in the rat pup vocalization model is also presented.

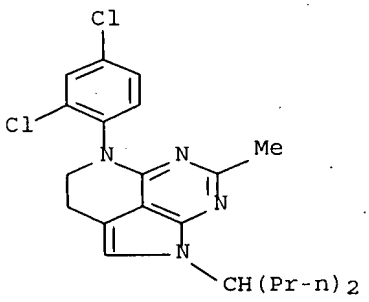
IT **862901-65-3P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(substituted tetraazaacenaphthylenes as potent CRF1 receptor antagonists for treatment of depression and anxiety)
RN 862901-65-3 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 1-(cyclopropylmethyl)-5-(2,4-dichlorophenyl)-1,3,4,5-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)



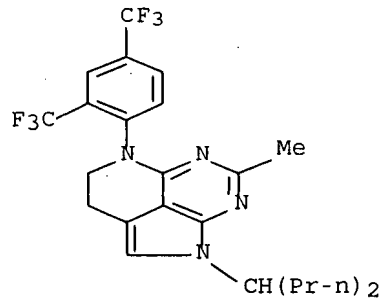
IT **862901-66-4P 862901-67-5P 862901-68-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(substituted tetraazaacenaphthylenes as potent CRF1 receptor antagonists for treatment of depression and anxiety)
RN 862901-66-4 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-(2,4-dichlorophenyl)-1-(1-ethylpropyl)-1,3,4,5-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)



RN 862901-67-5 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-(2,4-dichlorophenyl)-1,3,4,5-tetrahydro-7-methyl-1-(1-propylbutyl)- (9CI) (CA INDEX NAME)

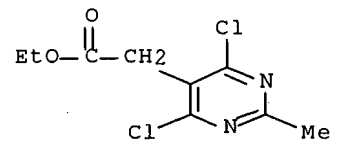


RN 862901-68-6 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-[2,4-bis(trifluoromethyl)phenyl]-1,3,4,5-tetrahydro-7-methyl-1-(1-propylbutyl)- (9CI) (CA INDEX NAME)

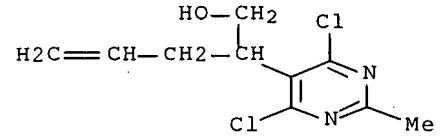


IT **175140-75-7P 474103-23-6P 474103-33-8P**
474103-39-4P 474103-40-7P 474103-59-8P
474103-60-1P 474103-65-6P 474103-66-7P
474103-67-8P 474103-69-0P 474103-81-6P
474103-88-3P 474103-94-1P 476645-16-6P
476645-20-2P 862901-60-8P 862901-61-9P
862901-62-0P 862901-63-1P 862901-64-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(substituted tetraazaacenaphthylenes as potent CRF1 receptor antagonists for treatment of depression and anxiety)

RN 175140-75-7 HCAPLUS
CN 5-Pyrimidineacetic acid, 4,6-dichloro-2-methyl-, ethyl ester (9CI) (CA INDEX NAME)

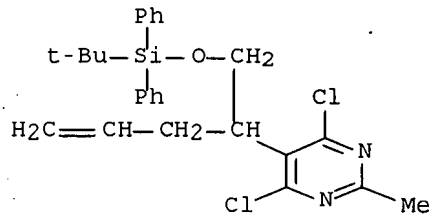


RN 474103-23-6 HCAPLUS
CN 5-Pyrimidineethanol, 4,6-dichloro-2-methyl-β-2-propenyl- (9CI) (CA INDEX NAME)

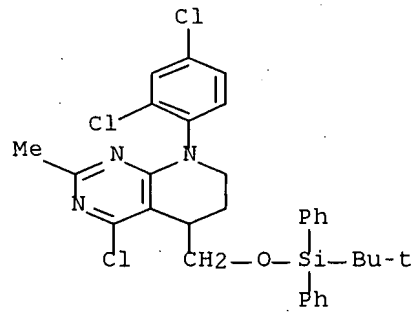


RN 474103-33-8 HCAPLUS
CN Pyrimidine, 4,6-dichloro-5-[1-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]meth

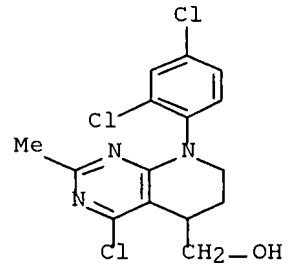
yl]-3-butenyl]-2-methyl- (9CI) (CA INDEX NAME)



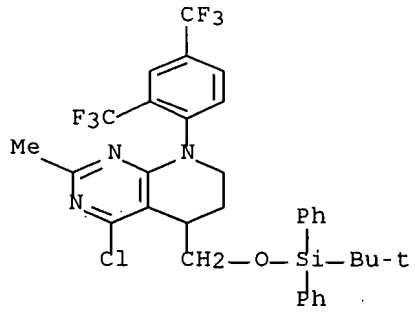
RN 474103-39-4 HCAPLUS
CN Pyrido[2,3-d]pyrimidine, 4-chloro-8-(2,4-dichlorophenyl)-5-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)



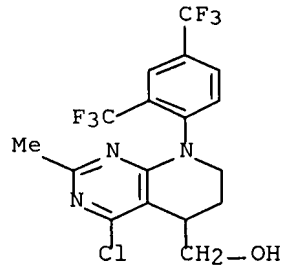
RN 474103-40-7 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 4-chloro-8-(2,4-dichlorophenyl)-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)



RN 474103-59-8 HCAPLUS
CN Pyrido[2,3-d]pyrimidine, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)

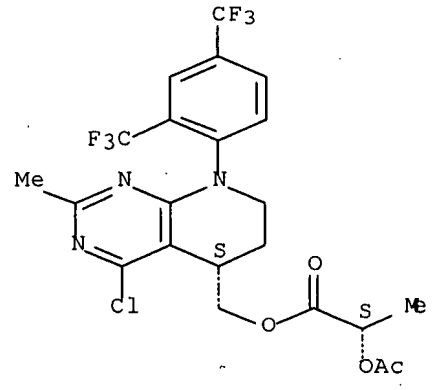


RN 474103-60-1 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)



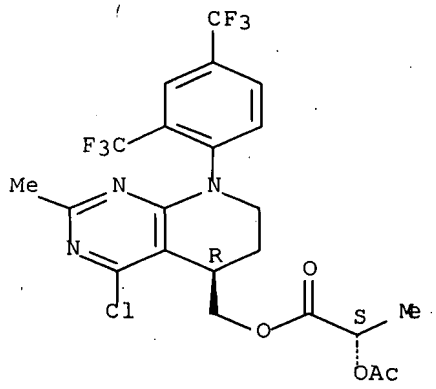
RN 474103-65-6 HCAPLUS
CN Propanoic acid, 2-(acetyloxy)-, [(5S)-8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methylpyrido[2,3-d]pyrimidin-5-yl]methyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



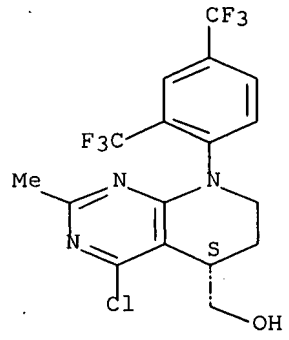
RN 474103-66-7 HCAPLUS
CN Propanoic acid, 2-(acetyloxy)-, [(5R)-8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methylpyrido[2,3-d]pyrimidin-5-yl]methyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



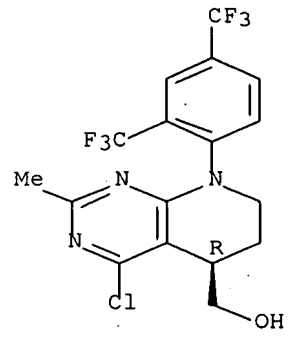
RN 474103-67-8 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methyl-, (5S)- (CA INDEX NAME)

Absolute stereochemistry.

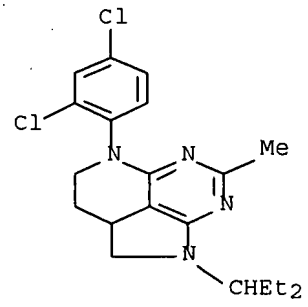


RN 474103-69-0 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methyl-, (5R)- (CA INDEX NAME)

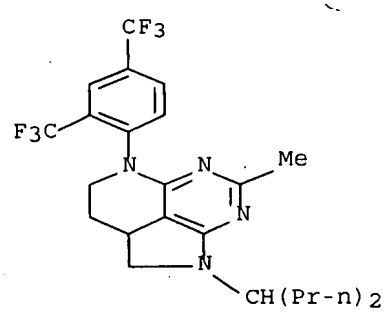
Absolute stereochemistry.



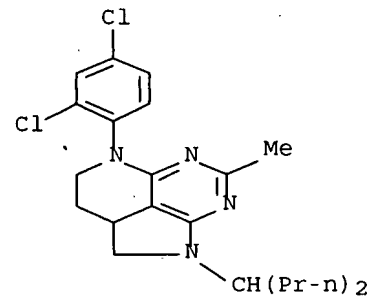
RN 474103-81-6 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-(2,4-dichlorophenyl)-1-(1-ethylpropyl)-1,2,2a,3,4,5-hexahydro-7-methyl- (9CI) (CA INDEX NAME)



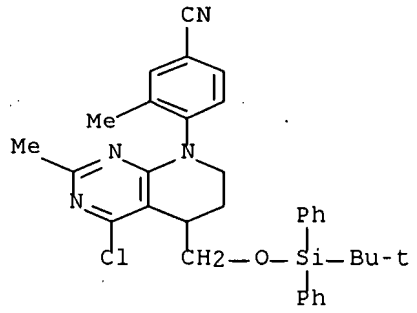
RN 474103-88-3 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-[2,4-bis(trifluoromethyl)phenyl]-1,2,2a,3,4,5-hexahydro-7-methyl-1-(1-propylbutyl)- (9CI) (CA INDEX NAME)



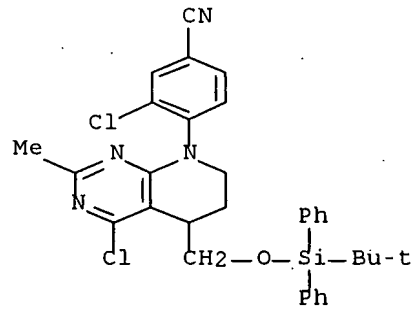
RN 474103-94-1 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-(2,4-dichlorophenyl)-1,2,2a,3,4,5-hexahydro-7-methyl-1-(1-propylbutyl)- (9CI) (CA INDEX NAME)



RN 476645-16-6 HCAPLUS
CN Benzonitrile, 4-[4-chloro-5-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7-dihydro-2-methylpyrido[2,3-d]pyrimidin-8(5H)-yl]-3-methyl- (CA INDEX NAME)

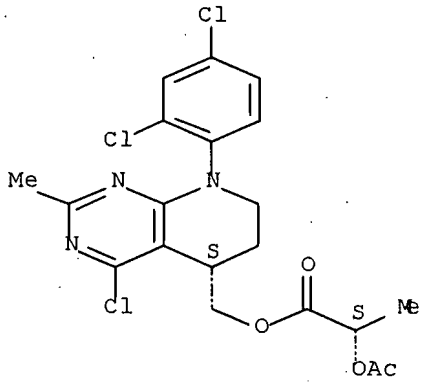


RN 476645-20-2 HCAPLUS
CN Benzonitrile, 3-chloro-4-[4-chloro-5-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7-dihydro-2-methylpyrido[2,3-d]pyrimidin-8(5H)-yl]- (CA INDEX NAME)



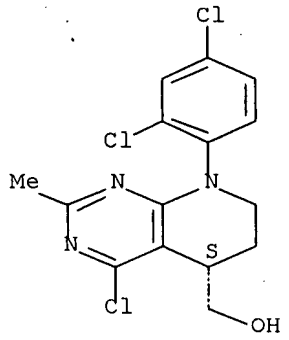
RN 862901-60-8 HCAPLUS
CN Propanoic acid, 2-(acetyloxy)-, [(5S)-4-chloro-8-(2,4-dichlorophenyl)-5,6,7,8-tetrahydro-2-methylpyrido[2,3-d]pyrimidin-5-yl]methyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



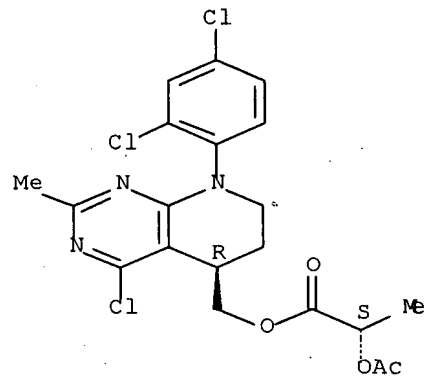
RN 862901-61-9 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 4-chloro-8-(2,4-dichlorophenyl)-5,6,7,8-tetrahydro-2-methyl-, (5S)- (CA INDEX NAME)

Absolute stereochemistry.



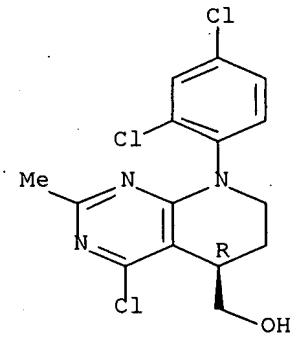
RN 862901-62-0 HCAPLUS
CN Propanoic acid, 2-(acetyloxy)-, [(5R)-4-chloro-8-(2,4-dichlorophenyl)-5,6,7,8-tetrahydro-2-methylpyrido[2,3-d]pyrimidin-5-yl]methyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

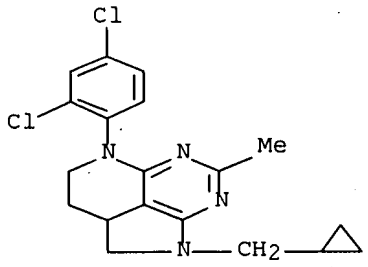


RN 862901-63-1 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 4-chloro-8-(2,4-dichlorophenyl)-5,6,7,8-tetrahydro-2-methyl-, (5R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 862901-64-2 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 1-(cyclopropylmethyl)-5-(2,4-dichlorophenyl)-1,2,2a,3,4,5-hexahydro-7-methyl- (9CI) (CA INDEX NAME)



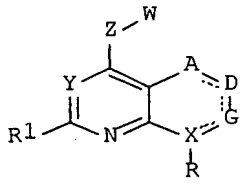
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:927206 HCAPLUS Full-text
DOCUMENT NUMBER: 141:395570
TITLE: Preparation of condensed heterocycles as CRF receptor antagonists for treatment of depression, anxiety, IBS, and IBD
INVENTOR(S): St.-Denis, Yves
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., USA; Neurocrine Biosciences Inc.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

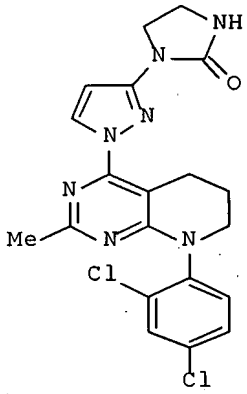
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094419	A1	20041104	WO 2004-IB1283	20040408
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1805958	A	20060719	CN 2004-80016189	20040407
EP 1618107	A1	20060125	EP 2004-726587	20040408
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2006522798	T	20061005	JP 2006-506536	20040408
US 2007021429	A1	20070125	US 2006-552494	20060801
PRIORITY APPLN. INFO.:			GB 2003-8208 A	20030409
			US 2003-485322P P	20030707
			WO 2004-IB1283 W	20040408

OTHER SOURCE(S): MARPAT 141:395570

GI



I



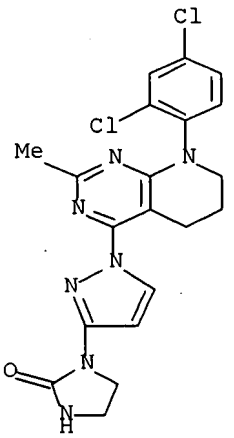
II

AB Title compds. I [wherein A = CR12R13, CR12; D = CR8R9, CR8; G = CR10R11, CR10; W = (un)substituted carbocyclyl with one C optionally replaced by SO0-2; X = C, N; Y = CR7; Z = (un)substituted heterocyclyl, Ph; R = (un)substituted (hetero)aryl; R1 = H, (cyclo)alkyl, (halo)alkoxy, alkylthio, alkenyl, alkynyl, halo(alkyl), halo, NR3R4, CN; R3, R4 = independently H, alkyl; R7 = H, (halo)alkyl, halo; R8-R13 = independently H, (cyclo)alkyl, alkenyl, alkynyl, NR3R4, CN; and stereoisomers, prodrugs and pharmaceutically acceptable salts, or solvates thereof] were prepared as corticotropin-releasing factor (CRF) antagonists. Examples include the syntheses for a [(pyrido[2,3-d]pyrimidinyl)pyrazolyl]imidazolidinone, a [(quinazolinyl)pyrazolyl]imidazolidinone, a [(naphthyridinyl)pyrazolyl]imidazolidinone, and their intermediates. For instance, 4-chloro-8-(2,4-dichlorophenyl)-2-methyl-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidine was coupled

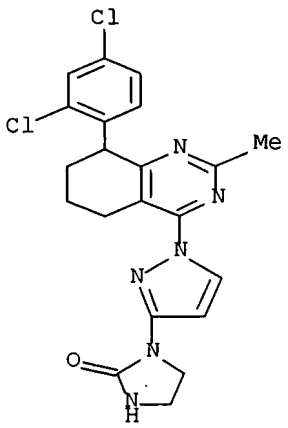
with 1-(1H-pyrazol-3-yl)imidazolidin-2-one (prepns. given) to afford II. In binding assays using recombinant human CRF1 and CRF2 receptors expressed in CHO cell membranes, compds. of the invention showed affinity for CRF receptors with Ki values of <10 μM.

IT **785834-48-2P**, 1-[1-[8-(2,4-Dichlorophenyl)-2-methyl-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-4-yl]-1H-pyrazol-3-yl]-2-imidazolidinone
785834-49-3P, 1-[1-[8-(2,4-Dichlorophenyl)-2-methyl-5,6,7,8-tetrahydroquinazolin-4-yl]-1H-pyrazol-3-yl]-2-imidazolidinone
785834-50-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CRF antagonist; preparation of condensed heterocycles as CRF receptor antagonists for treatment of depression, anxiety, IBS, and IBD)

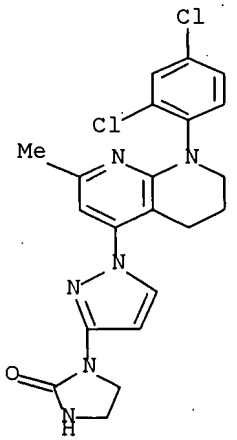
RN 785834-48-2 HCAPLUS
CN 2-Imidazolidinone, 1-[1-[8-(2,4-dichlorophenyl)-5,6,7,8-tetrahydro-2-methylpyrido[2,3-d]pyrimidin-4-yl]-1H-pyrazol-3-yl]- (CA INDEX NAME)



RN 785834-49-3 HCAPLUS
CN 2-Imidazolidinone, 1-[1-[8-(2,4-dichlorophenyl)-5,6,7,8-tetrahydro-2-methyl-4-quinazolinyl]-1H-pyrazol-3-yl]- (CA INDEX NAME)

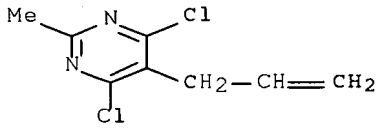


RN 785834-50-6 HCAPLUS
CN 2-Imidazolidinone, 1-[1-[8-(2,4-dichlorophenyl)-5,6,7,8-tetrahydro-2-methyl-1,8-naphthyridin-4-yl]-1H-pyrazol-3-yl]- (CA INDEX NAME)

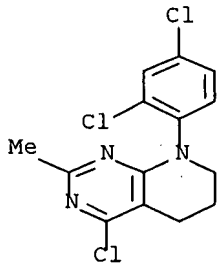


IT **85826-33-1P**, 4,6-Dichloro-2-methyl-5-(2-propen-1-yl)pyrimidine
474656-22-9P, 4-Chloro-8-(2,4-dichlorophenyl)-2-methyl-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**
(intermediate; preparation of condensed heterocycles as CRF receptor antagonists for treatment of depression, anxiety, IBS, and IBD)

RN 85826-33-1 HCAPLUS
CN Pyrimidine, 4,6-dichloro-2-methyl-5-(2-propen-1-yl)- (CA INDEX NAME)

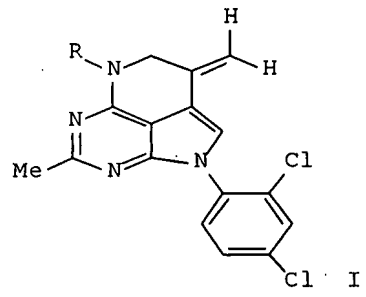


RN 474656-22-9 HCAPLUS
CN Pyrido[2,3-d]pyrimidine, 4-chloro-8-(2,4-dichlorophenyl)-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

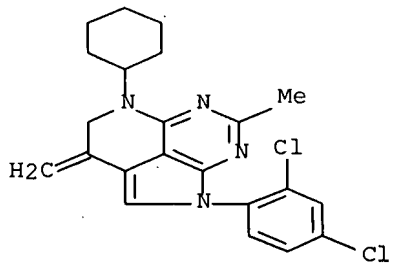
L20 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:15217 HCAPLUS Full-text
DOCUMENT NUMBER: 140:94007
TITLE: Synthesis of pyrrolopyrimidine CRF-R1 antagonists containing a tricyclic core via an intramolecular Heck reaction
AUTHOR(S): Dyck, Brian; McCarthy, James R.
CORPORATE SOURCE: Department of Medicinal Chemistry, Neurocrine Biosciences, Inc., San Diego, CA, 92121, USA
SOURCE: Heterocycles (2004), 62, 191-195
CODEN: HTCYAM; ISSN: 0385-5414
PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:94007
GI



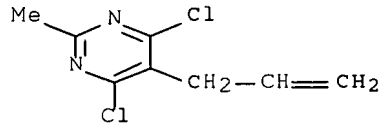
AB A synthetic route to pharmaceutically important tricyclic pyrrolopyrimidines I (R = Me, c-hexyl, 4-heptyl) has been developed. The method employed a palladium-mediated Heck cyclization as the critical step in the construction of the final six membered ring.

IT **644994-60-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and CRF-R1 antagonistic activity of piperidinopyrrolopyrimidines via intramol. Heck reaction of bromo(allylamino)pyrrolopyrimidines)

RN 644994-60-5 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-cyclohexyl-1-(2,4-dichlorophenyl)-1,3,4,5-tetrahydro-7-methyl-3-methylene- (9CI) (CA INDEX NAME)



IT **85826-33-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(preparation of bromopyrrolopyrimidines via heterocyclization of allylmalonate with acetamidine followed by chlorination, substitution with dichloroaniline, oxidative cleavage, heterocyclization, bromination, and substitution with amines)
RN 85826-33-1 HCAPLUS
CN Pyrimidine, 4,6-dichloro-2-methyl-5-(2-propen-1-yl)- (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:906225 HCAPLUS Full-text
DOCUMENT NUMBER: 138:4610
TITLE: Preparation of tri- and tetraazaacenaphthylenes as corticotropin releasing factor (CRF) receptor antagonists
INVENTOR(S): Di, Fabio Romano; Gentile, Gabriella; Haddach, Mustapha; St-denis, Yves; Williams, John Patrick
PATENT ASSIGNEE(S): Neurocrine Inc., USA; Sb Pharmco Puerto Rico Inc.; Di Fabio, Romano
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002094826		A1	20021128	WO 2002-GB2377	20020521
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2450535		A1	20021128	CA 2002-2450535	20020521
AU 2002257939		A1	20021203	AU 2002-257939	20020521
EP 1392689		A1	20040303	EP 2002-727742	20020521
EP 1392689		B1	20061025		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002009947		A	20040427	BR 2002-9947	20020521
HU 2004000854		A2	20040830	HU 2004-854	20020521
CN 1529705		A	20040915	CN 2002-813591	20020521
JP 2004530702		T	20041007	JP 2002-591499	20020521
NZ 529471		A	20051223	NZ 2002-529471	20020521
AT 343578		T	20061115	AT 2002-727742	20020521
ES 2274972		T3	20070601	ES 2002-2727742	20020521
ZA 2003008810		A	20041130	ZA 2003-8810	20031112
IN 2003DN01920		A	20070112	IN 2003-DN1920	20031114
MX 2003PA10635		A	20041206	MX 2003-PA10635	20031119
US 2004198726		A1	20041007	US 2004-477886	20040528
PRIORITY APPLN. INFO.:				US 2001-292660P	P 20010521
				WO 2002-GB2377	W 20020521

OTHER SOURCE(S): MARPAT 138:4610

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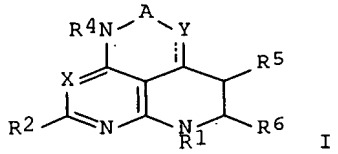
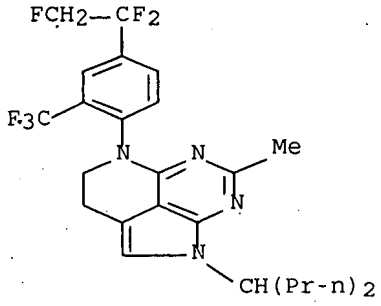


I

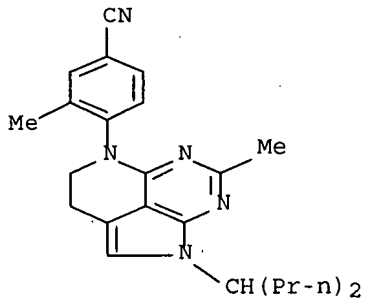
AB Title compds. [I; A = bond, C:Z; X = N, CR3; Y = N, NR7, CR8, O; Z = O, S, NR9; R1 = (substituted) alkyl, aryl, heteroaryl; R2 = H, (substituted) alkyl, alkoxy, thioalkyl, halo, cyano, haloalkyl; R3 = H, (substituted) alkyl, halo, haloalkyl; R4 = H, alkyl, substituted alkyl, COR1, (substituted) aryl, heterocyclyl; R5 = H, halo, (substituted) alkyl, aryl, heteroaryl, alkoxy, thioalkyl, COR1, NR10R11, cyano; R6 = H, halo, (substituted) alkyl, aryl, heteroaryl, alkoxy, thioalkyl, COR1, NR100R11, cyano; R7 = H, (substituted) alkyl, COR1, aryl, substituted aryl, heteroaryl; R8 = H, halo, (substituted) alkyl, aryl, heteroaryl, alkoxy, thioalkyl, alkylcarbonyl, NR10R11, cyano; R9 = H, (substituted) alkyl, aryl, heteroaryl; R10, R11 = H, (substituted) alkyl, aryl, heteroaryl], were prepared for treatment of stroke, depression, anxiety, irritable bowel syndrome, and inflammatory bowel disease (no data). Thus, 3-methyl-4-[7-methyl-1-(1-propylbutyl)-2,2a,3,4-tetrahydro-1H-1,5,6,8-tetraazaacenaphthylen-5-yl]benzonitrile (preparation given) was stirred with DDQ in CH2Cl2 to give 56% 3-methyl-4-[7-methyl-1-(1-propylbutyl)-3,4- dihydro-1H-1,5,6,8-tetraazaacenaphthylen-5-yl]benzonitrile.

IT **476645-06-4P 476645-07-5P 476645-08-6P**
476645-09-7P 476645-10-0P 476645-11-1P
476645-12-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of tri- and tetraazaacenaphthylenes as corticotropin releasing factor (CRF) receptor antagonists)

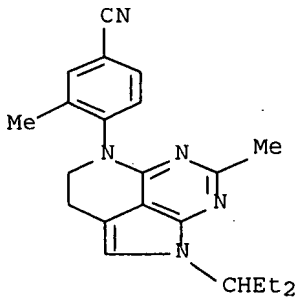
RN 476645-06-4 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 1,3,4,5-tetrahydro-7-methyl-1-(1-propylbutyl)-5-[4-(1,1,2-trifluoroethyl)-2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



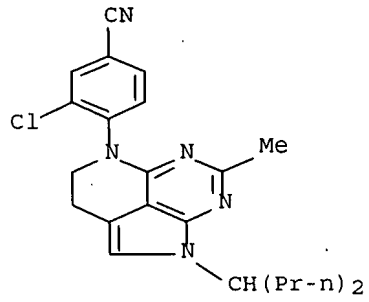
RN 476645-07-5 HCAPLUS
CN Benzonitrile, 4-[3,4-dihydro-7-methyl-1-(1-propylbutyl)-1,5,6,8-tetraazaacenaphthylen-5(1H)-yl]-3-methyl- (9CI) (CA INDEX NAME)



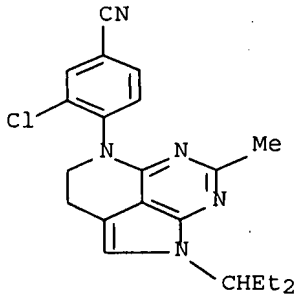
RN 476645-08-6 HCAPLUS
CN Benzonitrile, 4-[1-(1-ethylpropyl)-3,4-dihydro-7-methyl-1,5,6,8-tetraazaacenaphthylen-5(1H)-yl]-3-methyl- (9CI) (CA INDEX NAME)



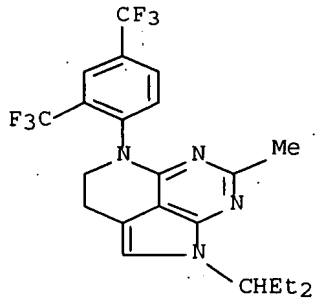
RN 476645-09-7 HCAPLUS
CN Benzonitrile, 3-chloro-4-[3,4-dihydro-7-methyl-1-(1-propylbutyl)-1,5,6,8-tetraazaacenaphthylen-5(1H)-yl]- (9CI) (CA INDEX NAME)



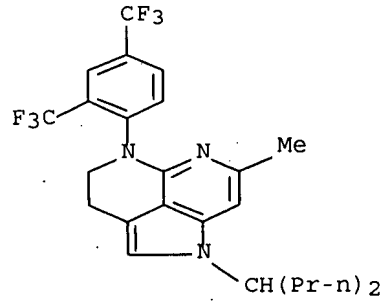
RN 476645-10-0 HCAPLUS
CN Benzonitrile, 3-chloro-4-[1-(1-ethylpropyl)-3,4-dihydro-7-methyl-1,5,6,8-tetraazaacenaphthylen-5(1H)-yl]- (9CI) (CA INDEX NAME)



RN 476645-11-1 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-[2,4-bis(trifluoromethyl)phenyl]-1-(1-ethylpropyl)-1,3,4,5-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)

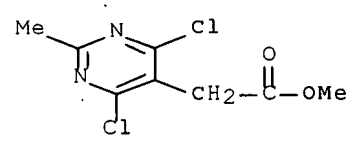


RN 476645-12-2 HCAPLUS
CN Pyrrolo[2,3,4-de]-1,8-naphthyridine, 8-[2,4-bis(trifluoromethyl)phenyl]-4,6,7,8-tetrahydro-2-methyl-4-(1-propylbutyl)- (CA INDEX NAME)



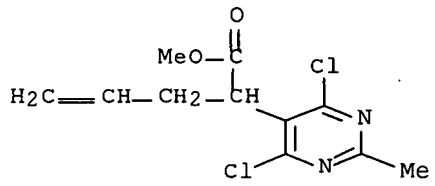
IT **142228-52-2P**, (4,6-Dichloro-2-methylpyrimidin-5-yl)acetic acid methyl ester **474103-22-5P 474103-23-6P 474103-33-8P 474103-59-8P 474103-60-1P 474103-88-3P 476645-13-3P 476645-14-4P 476645-15-5P 476645-16-6P 476645-17-7P 476645-18-8P 476645-19-9P 476645-20-2P 476645-21-3P 476645-22-4P 476645-23-5P 476645-24-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(preparation of tri- and tetraazaacenaphthylenes as corticotropin releasing factor (CRF) receptor antagonists)

RN 142228-52-2 HCAPLUS
CN 5-Pyrimidineacetic acid, 4,6-dichloro-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



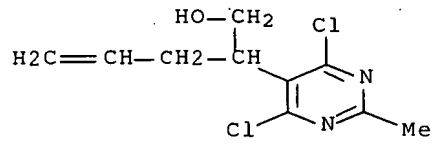
RN 474103-22-5 HCAPLUS

CN 5-Pyrimidineacetic acid, 4,6-dichloro-2-methyl-α-2-propenyl-, methyl ester (9CI) (CA INDEX NAME)



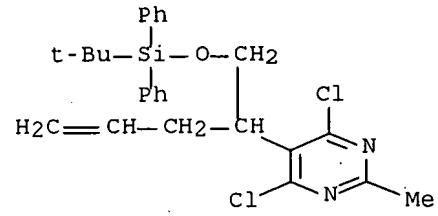
RN 474103-23-6 HCAPLUS

CN 5-Pyrimidineethanol, 4,6-dichloro-2-methyl-β-2-propenyl- (9CI) (CA INDEX NAME)



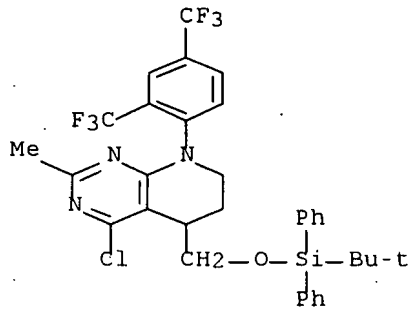
RN 474103-33-8 HCAPLUS

CN Pyrimidine, 4,6-dichloro-5-[1-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-3-butenyl]-2-methyl- (9CI) (CA INDEX NAME)

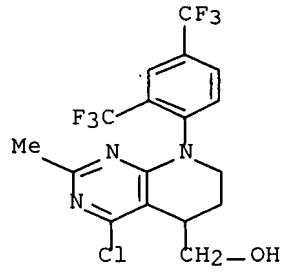


RN 474103-59-8 HCAPLUS

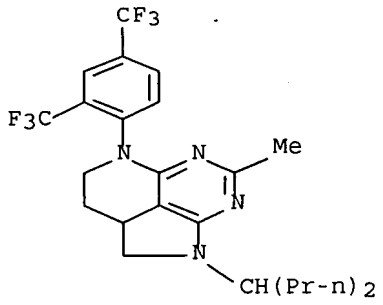
CN Pyrido[2,3-d]pyrimidine, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)



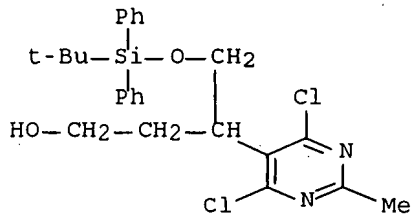
RN 474103-60-1 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)



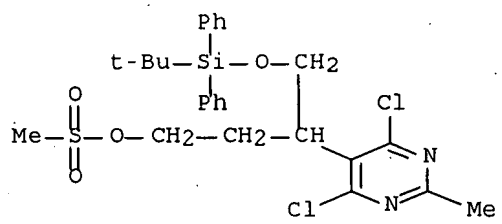
RN 474103-88-3 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-[2,4-bis(trifluoromethyl)phenyl]-1,2,2a,3,4,5-hexahydro-7-methyl-1-(1-propylbutyl)- (9CI) (CA INDEX NAME)



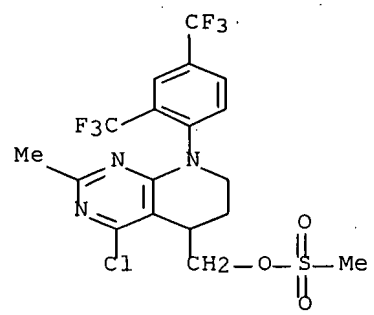
RN 476645-13-3 HCAPLUS
CN 5-Pyrimidinepropanol, 4,6-dichloro-γ-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-2-methyl- (CA INDEX NAME)



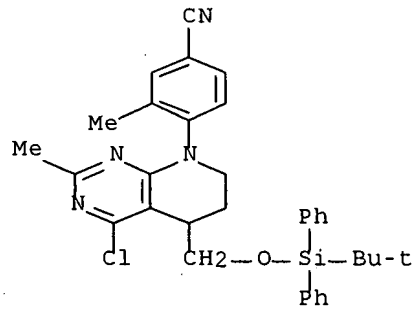
RN 476645-14-4 HCAPLUS
CN 5-Pyrimidinepropanol, 4,6-dichloro-γ-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-2-methyl-, methanesulfonate (ester) (9CI) (CA INDEX NAME)



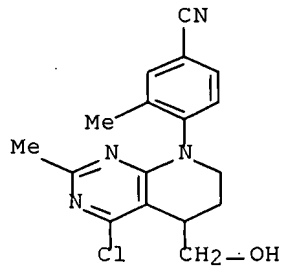
RN 476645-15-5 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methyl-, methanesulfonate (ester) (9CI) (CA INDEX NAME)



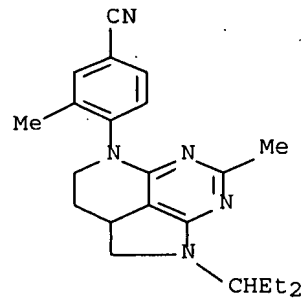
RN 476645-16-6 HCAPLUS
CN Benzonitrile, 4-[4-chloro-5-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7-dihydro-2-methylpyrido[2,3-d]pyrimidin-8(5H)-yl]-3-methyl- (CA INDEX NAME)



RN 476645-17-7 HCAPLUS
CN Benzonitrile, 4-[4-chloro-6,7-dihydro-5-(hydroxymethyl)-2-methylpyrido[2,3-d]pyrimidin-8(5H)-yl]-3-methyl- (CA INDEX NAME)



RN 476645-18-8 HCAPLUS
CN Benzonitrile, 4-[1-(1-ethylpropyl)-2,2a,3,4-tetrahydro-7-methyl-1,5,6,8-tetraazaacenaphthylen-5(1H)-yl]-3-methyl- (9CI) (CA INDEX NAME)



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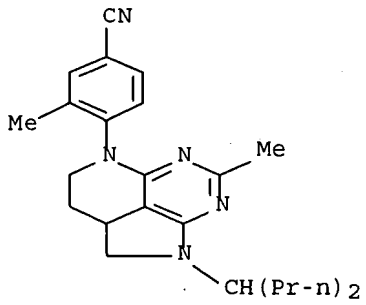
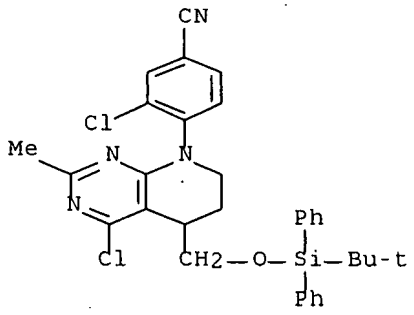
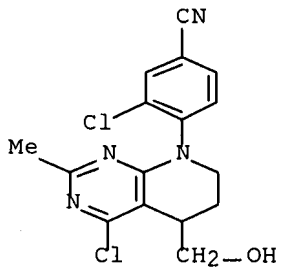
CN Benzonitrile, 3-methyl-4-[2,2a,3,4-tetrahydro-7-methyl-1-(1-propylbutyl)-1,5,6,8-tetraazaacenaphthylen-5(1H)-yl]- (9CI) (CA INDEX NAME)



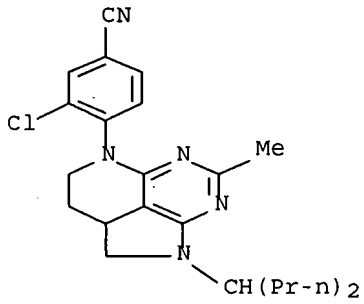
RN 476645-20-2 HCAPLUS
CN Benzonitrile, 3-chloro-4-[4-chloro-5-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7-dihydro-2-methylpyrido[2,3-d]pyrimidin-8(5H)-yl]- (CA INDEX NAME)



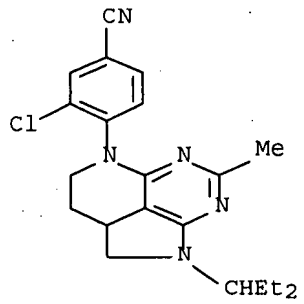
RN 476645-21-3 HCAPLUS
CN Benzonitrile, 3-chloro-4-[4-chloro-6,7-dihydro-5-(hydroxymethyl)-2-methylpyrido[2,3-d]pyrimidin-8(5H)-yl]- (CA INDEX NAME)



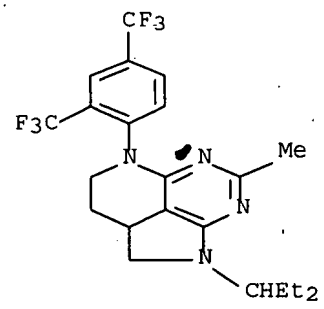
RN 476645-22-4 HCAPLUS
CN Benzonitrile, 3-chloro-4-[2,2a,3,4-tetrahydro-7-methyl-1-(1-propylbutyl)-1,5,6,8-tetraazaacenaphthylen-5(1H)-yl]- (9CI) (CA INDEX NAME)



RN 476645-23-5 HCAPLUS
CN Benzonitrile, 3-chloro-4-[1-(1-ethylpropyl)-2,2a,3,4-tetrahydro-7-methyl-1,5,6,8-tetraazaacenaphthylen-5(1H)-yl]- (9CI) (CA INDEX NAME)



RN 476645-24-6 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-[2,4-bis(trifluoromethyl)phenyl]-1-(1-ethylpropyl)-1,2,2a,3,4,5-hexahydro-7-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:849602 HCAPLUS Full-text
DOCUMENT NUMBER: 137:353055
TITLE: Preparation of fused pyrimidines as antagonists of

corticotropin releasing factor (CRF).

INVENTOR(S): Capelli, Anna Maria; Marchionni, Chiara; Micheli, Fabrizio; Pasquarello, Alessandra; Perini, Benedetta; St-Denis, Yves

PATENT ASSIGNEE(S): Glaxo Group Limited, UK; Di Fabio, Romano

SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088095	A1	20021107	WO 2002-GB2029	20020430
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2446514	A1	20021107	CA 2002-2446514	20020430
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EP 1383747	A1	20040128	EP 2002-722478	20020430
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HU 2003004054	A2	20040428	HU 2003-4054	20020430
BR 2002009267	A	20040615	BR 2002-9267	20020430
JP 2004528349	T	20040916	JP 2002-585397	20020430
CN 1649848	A	20050803	CN 2002-810746	20020430
IN 2003DN01499	A	20070112	IN 2003-DN1499	20030919
ZA 2003007367	A	20040421	ZA 2003-7367	20030922
NO 2003004836	A	20031029	NO 2003-4836	20031029
MX 2003PA09938	A	20050907	MX 2003-PA9938	20031029
US 2004176400	A1	20040909	US 2004-476368	20040416
US 7279474	B2	20071009		

PRIORITY APPLN. INFO.:		
GB 2001-10567	A	20010430
GB 2001-10569	A	20010430
GB 2001-10570	A	20010430
GB 2001-17399	A	20010717
GB 2001-17401	A	20010717
GB 2001-17420	A	20010717
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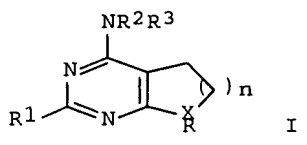
OTHER SOURCE(S): MARPAT 137:353055

GI

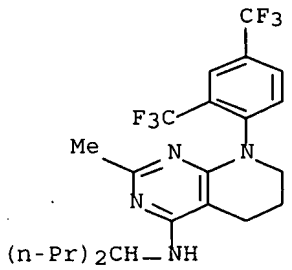


I

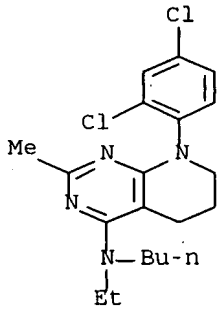
AB Title compds. [I; R = aryl, heteroaryl, which may be substituted by 1-4 halo, alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, haloalkoxy, COR4, NO2, NR9R10, cyano, R5; R1 = H, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, halo, NR9R10, cyano; R2 = H, cycloalkyl, R6; R3 = R2, but R2 and R3 may not be simultaneously H ; or R2R3N = saturated or unsatd. heterocycle, which may be substituted by 1-3 R7 groups; or R2R3N = 5-10 membered heteroaryl group, in which the 5-membered heteroaryl group contains ≥1 O, S, N and the heteroaryl contains 1-3 N atoms and wherein said 5-10 membered heteroaryl may be substituted by 1-3 R7; R4 = alkyl, OR9, NR9R10; R5 = 5-6 membered heterocycle, which may be saturated or may contain 1-3 double bonds, and which may be substituted by ≥1 R8; R6 = alkyl that may be substituted by ≥1 cycloalkyl, alkoxy, haloalkoxy, OH, haloalkyl; R7 = R5, 1R6, cycloalkyl, alkoxy, OH, halo, NO2, cyano, CONR9R10, Ph which may be substituted by 1-4 R8; R8 = alkyl, haloalkyl, halo, NO2, alkoxy, cyano; R9, R10 = H, alkyl; X = C, N; n = 1,2], were prepared Thus, 4-chloro-7-(2,4-dichlorophenyl)-2-methyl-6,7-dihydro-5H-pyrrolo[2,3- d]pyrimidine (preparation given) was heated with 1-ethylaminopropane at 140° in a sealed vial for 18 h to give [7-(2,4-dichlorophenyl)-2- methyl-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidin-4-yl](1-ethylpropyl)amine. I showed CRF binding activity with Ki<10 μM.

IT **474655-93-1P**, [8-(2,4-Bis-trifluoromethylphenyl)-2-methyl-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-4-yl](1-propylbutyl)amine **474655-94-2P**, N-Butyl-N-[8-(2,4-dichlorophenyl)-2-methyl-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-4-yl]-N-ethylamine **474655-95-3P**, N-(Cyclopropylmethyl)-N-[8-(2,4-dichlorophenyl)-2-methyl-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-4-yl]-N-propylamine **474657-20-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused pyrimidines as antagonists of corticotropin releasing factor (CRF))

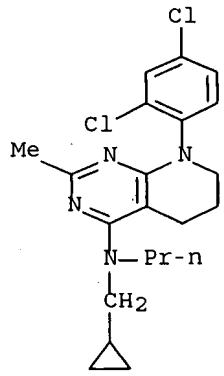
RN 474655-93-1 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-4-amine, 8-[2,4-bis(trifluoromethyl)phenyl]-5,6,7,8-tetrahydro-2-methyl-N-(1-propylbutyl)- (CA INDEX NAME)



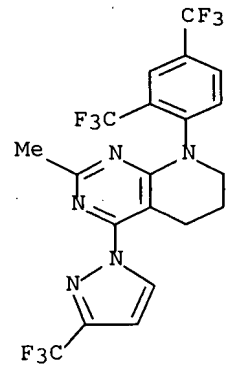
RN 474655-94-2 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-4-amine, N-butyl-8-(2,4-dichlorophenyl)-N-ethyl-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)



RN 474655-95-3 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-4-amine, N-(cyclopropylmethyl)-8-(2,4-dichlorophenyl)-5,6,7,8-tetrahydro-2-methyl-N-propyl- (CA INDEX NAME)



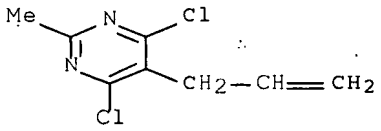
RN 474657-20-0 HCAPLUS
CN Pyrido[2,3-d]pyrimidine, 8-[2,4-bis(trifluoromethyl)phenyl]-5,6,7,8-tetrahydro-2-methyl-4-[3-(trifluoromethyl)-1H-pyrazol-1-yl]- (CA INDEX NAME)



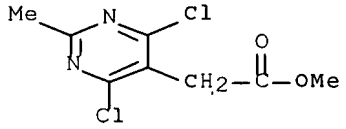
IT **85826-33-1P**, 5-Allyl-4,6-dichloro-2-methylpyrimidine
142228-52-2P, (4,6-Dichloro-2-methylpyrimidin-5-yl)acetic acid

methyl ester **474656-22-9P**, 4-Chloro-8-(2,4-dichlorophenyl)-2-methyl-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidine **474656-37-6P**, 2-(4,6-Dichloro-2-methylpyrimidin-5-yl)acetaldehyde **474656-38-7P**, 4,6-Dichloro-5-(3-methoxyallyl)-2-methylpyrimidine **474656-39-8P**, 3-(4,6-Dichloro-2-methylpyrimidin-5-yl)propionaldehyde **474656-40-1P**, 3-(4,6-Dichloro-2-methylpyrimidin-5-yl)propan-1-ol **474656-41-2P 474656-42-3P 474656-43-4P**, 2-(4,6-Dichloro-2-methylpyrimidin-5-yl)ethanol **474656-44-5P**, 5-[2-(tert-Butyldimethylsilanoxy)ethyl]-4,6-dichloro-2-methylpyrimidine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(preparation of fused pyrimidines as antagonists of corticotropin releasing factor (CRF))

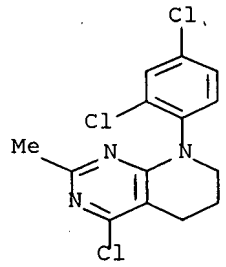
RN 85826-33-1 HCAPLUS
CN Pyrimidine, 4,6-dichloro-2-methyl-5-(2-propen-1-yl)- (CA INDEX NAME)



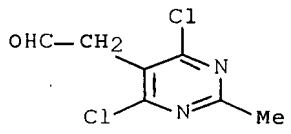
RN 142228-52-2 HCAPLUS
CN 5-Pyrimidineacetic acid, 4,6-dichloro-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



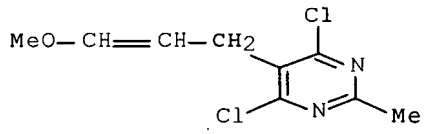
RN 474656-22-9 HCAPLUS
CN Pyrido[2,3-d]pyrimidine, 4-chloro-8-(2,4-dichlorophenyl)-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)



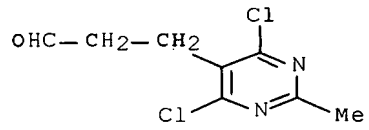
RN 474656-37-6 HCAPLUS
CN 5-Pyrimidineacetaldehyde, 4,6-dichloro-2-methyl- (CA INDEX NAME)



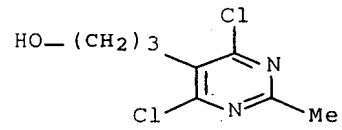
RN 474656-38-7 HCAPLUS
CN Pyrimidine, 4,6-dichloro-5-(3-methoxy-2-propenyl)-2-methyl- (9CI) (CA INDEX NAME)



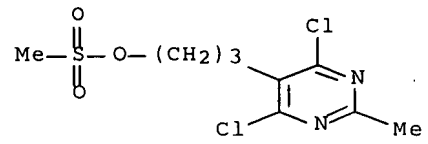
RN 474656-39-8 HCAPLUS
CN 5-Pyrimidinepropanal, 4,6-dichloro-2-methyl- (CA INDEX NAME)



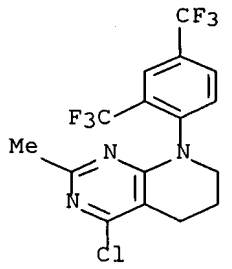
RN 474656-40-1 HCAPLUS
CN 5-Pyrimidinepropanol, 4,6-dichloro-2-methyl- (CA INDEX NAME)



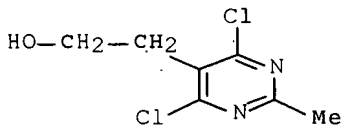
RN 474656-41-2 HCAPLUS
CN 5-Pyrimidinepropanol, 4,6-dichloro-2-methyl-, methanesulfonate (ester) (9CI) (CA INDEX NAME)



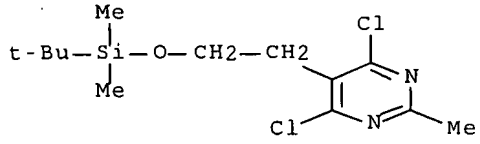
RN 474656-42-3 HCAPLUS
CN Pyrido[2,3-d]pyrimidine, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)



RN 474656-43-4 HCAPLUS
CN 5-Pyrimidineethanol, 4,6-dichloro-2-methyl- (CA INDEX NAME)



RN 474656-44-5 HCAPLUS
CN Pyrimidine, 4,6-dichloro-5-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethyl]-2-methyl- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:849430 HCAPLUS Full-text
DOCUMENT NUMBER: 137:337915
TITLE: Preparation of fused tricyclic quinazoline derivatives as CRF receptor antagonists
INVENTOR(S): Di Fabio, Romano; Micheli, Fabrizio; Pasquarello, Alessandra; St-Denis, Yves
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002087573	A1	20021107	WO 2002-GB1981	20020430
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
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CA 2446497	A1	20021107	CA 2002-2446497	20020430
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EP 1383498	B1	20060315		
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HU 2003004035	A2	20040428	HU 2003-4035	20020430
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NZ 528364	A	20051223	NZ 2002-528364	20020430
AT 320254	T	20060415	AT 2002-718405	20020430
ES 2255610	T3	20060701	ES 2002-2718405	20020430
IN 2003DN01498	A	20070316	IN 2003-DN1498	20030919
ZA 2003007368	A	20040503	ZA 2003-7368	20030922
NO 2003004837	A	20031209	NO 2003-4837	20031029
MX 2003PA09930	A	20040129	MX 2003-PA9930	20031029
US 2004235871	A1	20041125	US 2004-476441	20040528
PRIORITY APPLN. INFO.:			GB 2001-10566 A	20010430
			GB 2001-10579 A	20010430
			GB 2001-17423 A	20010717
			GB 2002-3203 A	20020211
			WO 2002-GB1981 W	20020430

OTHER SOURCE(S): MARPAT 137:337915
GI

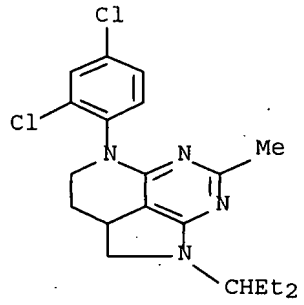
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R = (hetero)aryl; R1 = H, alk(en/yn)yl, haloalkyl, haloalkoxy, amino, cyano; R2 = H, alkyl; R3 = H, alk(en/yn)yl; Y, X = C, N; m, n = 0-1] were prepared For instance, 6-Dichloro-2-methylpyrimidin-5- yl was protected as the TBDMS-ether and subjected to the following sequence: i. THF, NaH, 2,4-dichloroaniline; ii. CH2Cl2, Boc2O, DMAP, 16 h; iii. CH2Cl2/MeOH, O3, NaBH4; iv. CH2Cl2, Et3N, MsCl; v. CH2Cl2, TFA; vi. THF, Et3N; vii. (DMF, Na2CO3, 4 H), Et3N•3HF; and viii. CH2Cl2, MsCl, Et3N to give II. II was treated with 3-pentylamine (120°, 8 h) to give example compound III. III had Ki < 0.1 μM for the CRF receptor. I are useful for the treatment of irritable bowel syndrome and depression.

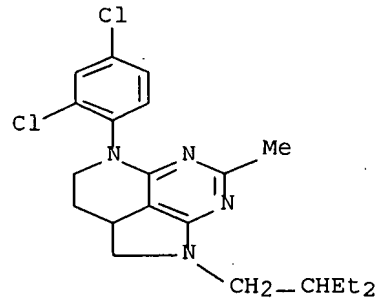
IT **474103-81-6P 474103-83-8P 474103-84-9P**
474103-88-3P 474103-90-7P 474103-91-8P
474103-94-1P 474103-96-3P 474103-97-4P
474104-21-7P 474104-22-8P 474104-23-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused tricyclic quinazoline (tetra-aza-acenaphthylene) derivs. as CRF receptor antagonists)

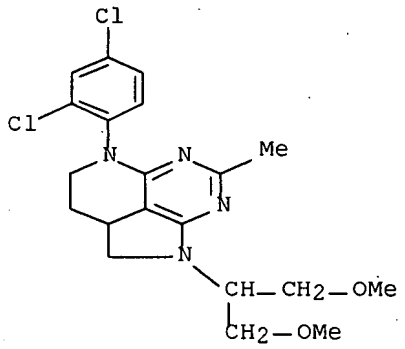
RN 474103-81-6 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-(2,4-dichlorophenyl)-1-(1-ethylpropyl)-1,2,2a,3,4,5-hexahydro-7-methyl- (9CI) (CA INDEX NAME)



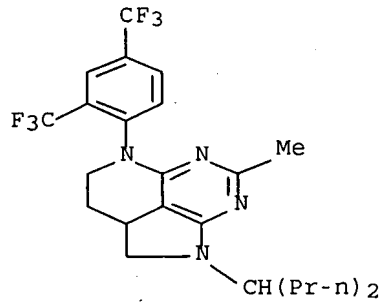
RN 474103-83-8 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-(2,4-dichlorophenyl)-1-(2-ethylbutyl)-1,2,2a,3,4,5-hexahydro-7-methyl- (9CI) (CA INDEX NAME)



RN 474103-84-9 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-(2,4-dichlorophenyl)-1,2,2a,3,4,5-hexahydro-1-[2-methoxy-1-(methoxymethyl)ethyl]-7-methyl- (9CI) (CA INDEX NAME)

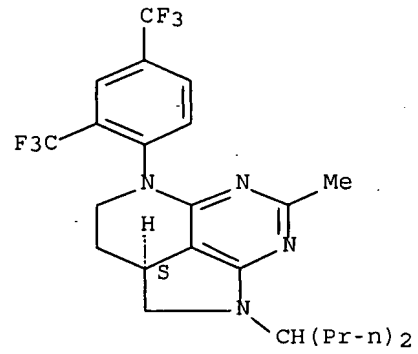


RN 474103-88-3 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-[2,4-bis(trifluoromethyl)phenyl]-1,2,2a,3,4,5-hexahydro-7-methyl-1-(1-propylbutyl)- (9CI) (CA INDEX NAME)



RN 474103-90-7 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-[2,4-bis(trifluoromethyl)phenyl]-1,2,2a,3,4,5-hexahydro-7-methyl-1-(1-propylbutyl)-, (2aS)- (9CI) (CA INDEX NAME)

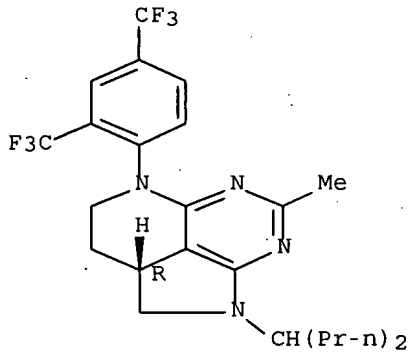
Absolute stereochemistry.



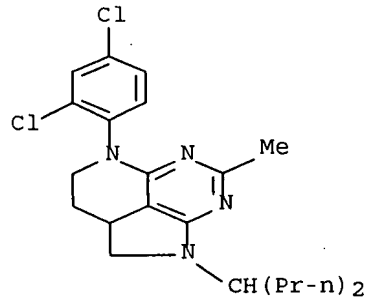
RN 474103-91-8 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-[2,4-bis(trifluoromethyl)phenyl]-1,2,2a,3,4,5-hexahydro-7-methyl-1-(1-propylbutyl)-, (2aR)- (9CI) (CA

INDEX NAME)

Absolute stereochemistry.

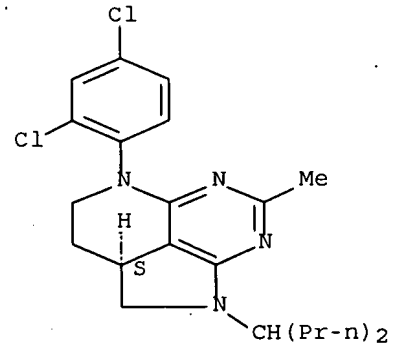


RN 474103-94-1 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-(2,4-dichlorophenyl)-1,2,2a,3,4,5-hexahydro-7-methyl-1-(1-propylbutyl)- (9CI) (CA INDEX NAME)



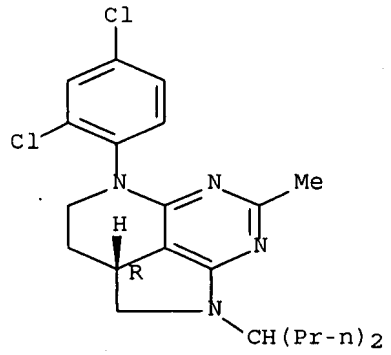
RN 474103-96-3 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-(2,4-dichlorophenyl)-1,2,2a,3,4,5-hexahydro-7-methyl-1-(1-propylbutyl)-, (2aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

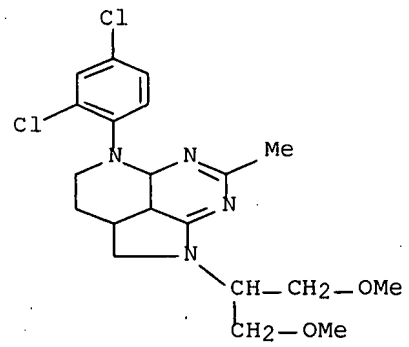


RN 474103-97-4 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-(2,4-dichlorophenyl)-1,2,2a,3,4,5-hexahydro-7-methyl-1-(1-propylbutyl)-, (2aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

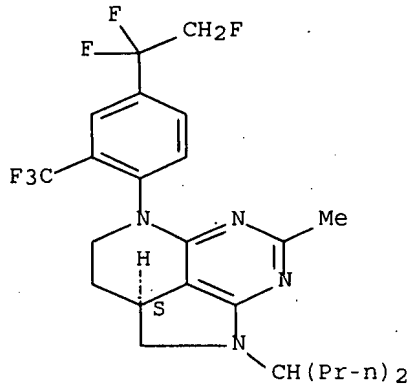


RN 474104-21-7 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-(2,4-dichlorophenyl)-1,2,2a,3,4,5,5a,8b-octahydro-1-[2-methoxy-1-(methoxymethyl)ethyl]-7-methyl- (9CI) (CA INDEX NAME)



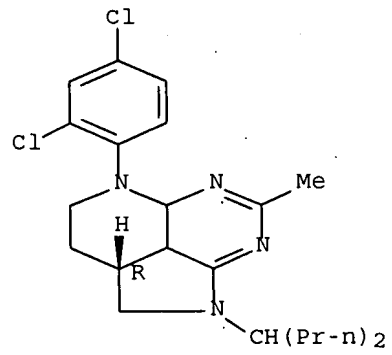
RN 474104-22-8 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 1,2,2a,3,4,5-hexahydro-7-methyl-1-(1-propylbutyl)-5-[4-(1,1,2-trifluoroethyl)-2-(trifluoromethyl)phenyl]-, (2aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 474104-23-9 HCAPLUS
CN 1,5,6,8-Tetraazaacenaphthylene, 5-(2,4-dichlorophenyl)-1,2,2a,3,4,5,5a,8b-octahydro-7-methyl-1-(1-propylbutyl)-, (2aR)- (9CI) (CA INDEX NAME)

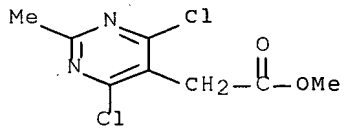
Absolute stereochemistry.



IT **142228-52-2P**, (4,6-Dichloro-2-methylpyrimidin-5-yl)acetic acid methyl ester **474103-22-5P**, 2-(4,6-Dichloro-2-methylpyrimidin-5-yl)pent-4-enoic acid methyl ester **474103-23-6P**, 2-(4,6-Dichloro-2-methylpyrimidin-5-yl)pent-4-en-1-ol **474103-24-7P**, 5-[1-(tert-Butyldimethylsilanyloxymethyl)but-3-enyl]-4,6-dichloro-2-methylpyrimidine **474103-33-8P**, 5-[1-((tert-Butyldiphenylsilanyloxy)methyl)but-3-enyl]-4,6-dichloro-2-methylpyrimidine **474103-39-4P**, 5-((tert-Butyldiphenylsilanyloxy)methyl)-4-chloro-8-(2,4-dichlorophenyl)-2-methyl-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidine **474103-40-7P**, [4-Chloro-8-(2,4-dichlorophenyl)-2-methyl-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-5-yl]methanol **474103-42-9P** **474103-58-7P**, 5-((tert-Butyldiphenylsilanyloxy)methyl)-4-chloro-2-methyl-8-[2,4-bis(trifluoromethyl)phenyl]-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-7-ol **474103-59-8P**, 5-((tert-Butyldiphenylsilanyloxy)methyl)-4-chloro-2-methyl-8-[2,4-bis(trifluoromethyl)phenyl]-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidine **474103-60-1P**, [4-Chloro-2-methyl-8-[2,4-bis(trifluoromethyl)phenyl]-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-5-yl]methanol **474103-61-2P**, Methanesulfonic acid 4-chloro-2-methyl-8-[2,4-bis(trifluoromethyl)phenyl]-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-5-ylmethyl ester **474103-65-6P**

474103-66-7P 474103-67-8P, (S)-[4-Chloro-2-methyl-8-[2,4-bis(trifluoromethyl)phenyl]-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-5-yl]methanol **474103-68-9P**, (S)-Methanesulfonic acid [4-chloro-2-methyl-8-[2,4-bis(trifluoromethyl)phenyl]-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-5-yl]methyl ester **474103-69-0P**, (R)-[4-Chloro-2-methyl-8-[2,4-bis(trifluoromethyl)phenyl]-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-5-yl]methanol **474103-71-4P**, (R)-Methanesulfonic acid [4-chloro-2-methyl-8-[2,4-bis(trifluoromethyl)phenyl]-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-5-yl]methyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**
(preparation of fused tricyclic quinazoline (tetra-aza-acenaphthylene) derivs. as CRF receptor antagonists)

RN 142228-52-2 HCAPLUS
CN 5-Pyrimidineacetic acid, 4,6-dichloro-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 474103-22-5 HCAPLUS
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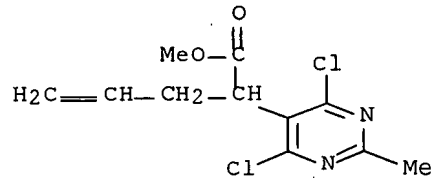
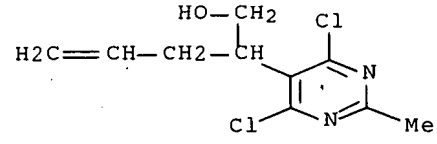
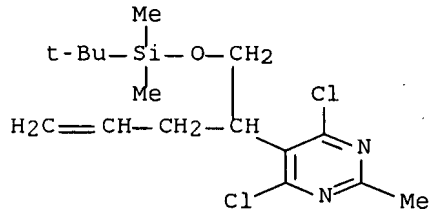


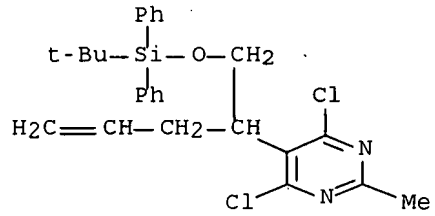
RN 474103-23-6 HCAPLUS
CN 5-Pyrimidineethanol, 4,6-dichloro-2-methyl-β-2-propenyl- (9CI) (CA INDEX NAME)



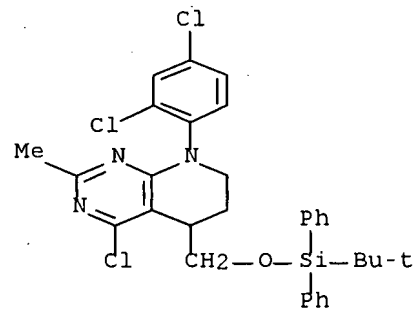
RN 474103-24-7 HCAPLUS
CN Pyrimidine, 4,6-dichloro-5-[1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-butenyl]-2-methyl- (9CI) (CA INDEX NAME)



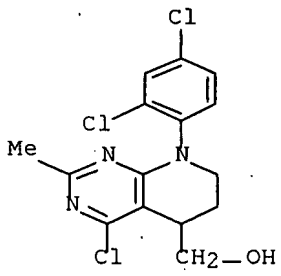
RN 474103-33-8 HCAPLUS
CN Pyrimidine, 4,6-dichloro-5-[1-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-3-butenyl]-2-methyl- (9CI) (CA INDEX NAME)



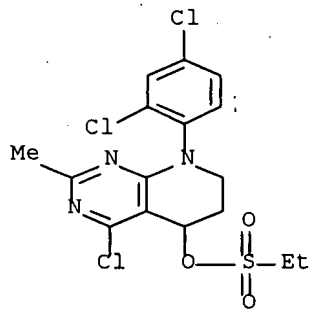
RN 474103-39-4 HCAPLUS
CN Pyrido[2,3-d]pyrimidine, 4-chloro-8-(2,4-dichlorophenyl)-5-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)



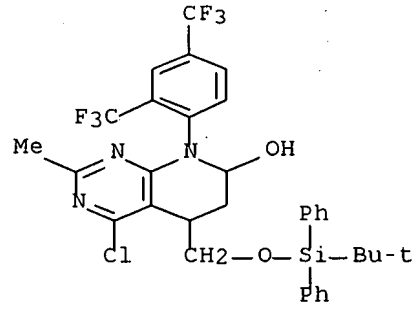
RN 474103-40-7 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 4-chloro-8-(2,4-dichlorophenyl)-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)



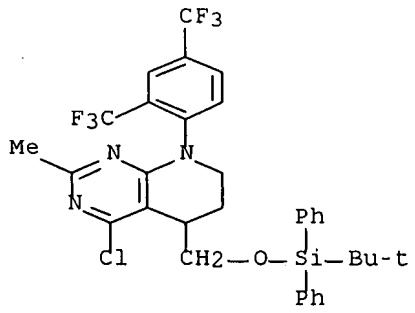
RN 474103-42-9 HCAPLUS
CN Ethanesulfonic acid, 4-chloro-8-(2,4-dichlorophenyl)-5,6,7,8-tetrahydro-2-methylpyrido[2,3-d]pyrimidin-5-yl ester (CA INDEX NAME)



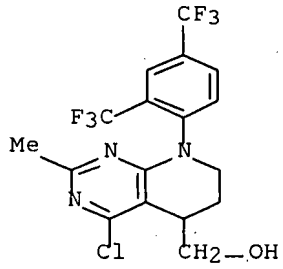
RN 474103-58-7 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7-ol, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)



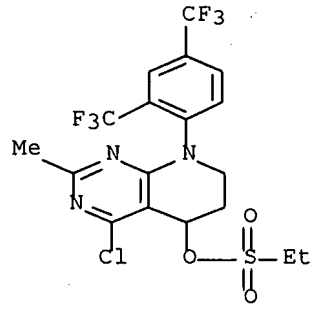
RN 474103-59-8 HCAPLUS
CN Pyrido[2,3-d]pyrimidine, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)



RN 474103-60-1 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methyl- (CA INDEX NAME)

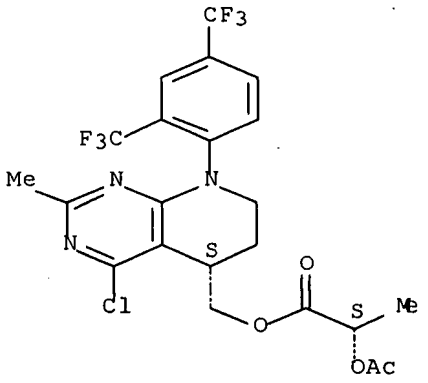


RN 474103-61-2 HCAPLUS
CN Ethanesulfonic acid, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methylpyrido[2,3-d]pyrimidin-5-yl ester (CA INDEX NAME)



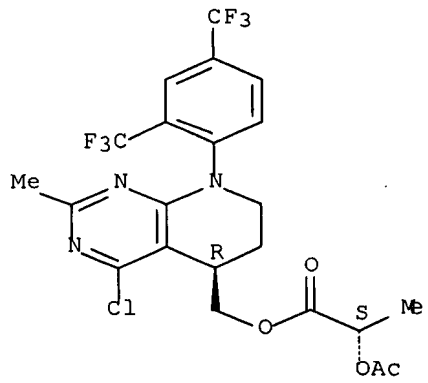
RN 474103-65-6 HCAPLUS
CN Propanoic acid, 2-(acetyloxy)-, [(5S)-8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methylpyrido[2,3-d]pyrimidin-5-yl]methyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



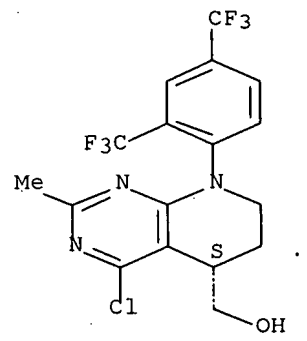
RN 474103-66-7 HCAPLUS
CN Propanoic acid, 2-(acetyloxy)-, [(5R)-8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methylpyrido[2,3-d]pyrimidin-5-yl]methyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



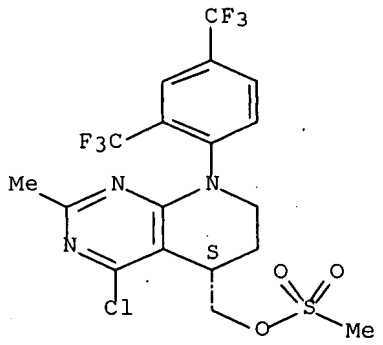
RN 474103-67-8 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methyl-, (5S)- (CA INDEX NAME)

Absolute stereochemistry.



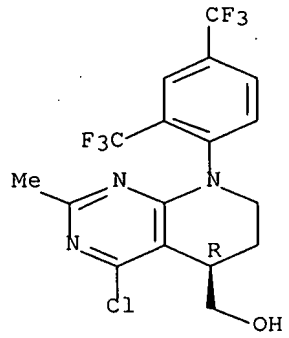
RN 474103-68-9 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methyl-, methanesulfonate (ester), (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



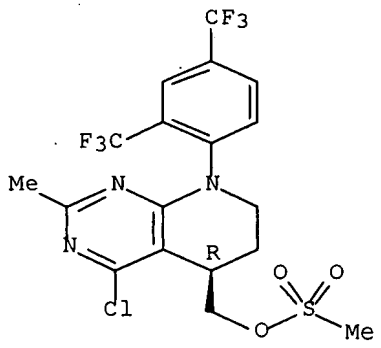
RN 474103-69-0 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methyl-, (5R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 474103-71-4 HCAPLUS
CN Pyrido[2,3-d]pyrimidine-5-methanol, 8-[2,4-bis(trifluoromethyl)phenyl]-4-chloro-5,6,7,8-tetrahydro-2-methyl-, methanesulfonate (ester), (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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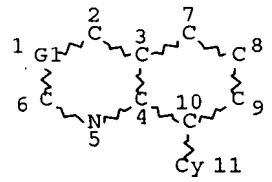
L2 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
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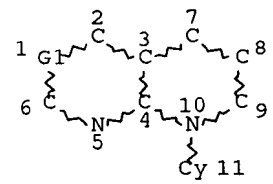
L4 STR



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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
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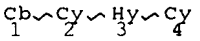
STEREO ATTRIBUTES: NONE
L5 11336 SEA FILE=REGISTRY SSS FUL L4
L6 STR



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GGCAT IS PCY AT 3
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 4

STEREO ATTRIBUTES: NONE
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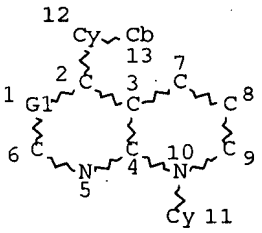
L9 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE
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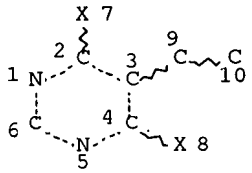
L12 14 SEA FILE=HCAPLUS ABB=ON PLU=ON L11
L13 STR



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NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

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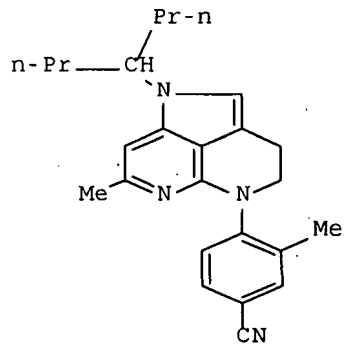
L22 ANSWER 1 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:923584 HCAPLUS Full-text
DOCUMENT NUMBER: 147:356365
TITLE: Novel substituted tetrahydrotriazaacenaphthylene derivatives as potent CRF1 receptor antagonists
AUTHOR(S): Gentile, Gabriella; Di Fabio, Romano; Pavone, Francesca; Sabbatini, Fabio Maria; **St-Denis, Yves**; Zampori, Maria Grazia; Vitulli, Giovanni; Worby, Angela
CORPORATE SOURCE: Medicine Research Centre, Psychiatry Centre of Excellence for Drug Discovery, GlaxoSmithkline, Verona, 37135, Italy
SOURCE: Bioorganic & Medicinal Chemistry Letters (2007), 17(18), 5218-5221
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

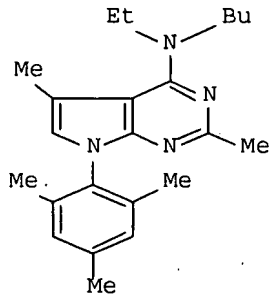


I

AB Corticotropin-releasing factor (CRF), a 41 amino acid peptide neurohormone synthesized by specific hypothalamic nuclei in the brain, is implicated in stress-related function. Antagonism of CRF1 receptors is an attractive therapeutic approach for the treatment of depression and anxiety. Unsatd. tetrahydrotriazaacenaphthylenes, and, in particular 3b (I), have been identified as potent and selective CRF1 receptor antagonists with a suitable oral pharmacokinetic profile.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:489050 HCAPLUS Full-text
DOCUMENT NUMBER: 146:513735
TITLE: Cyclopenta[d]pyrimidines and dihydropyrrolo[2,3-d]pyrimidines as potent and selective corticotropin-releasing factor 1 receptor antagonists
AUTHOR(S): Arban, Roberto; Benedetti, Roberto; Bonanomi, Giorgio; Capelli, Anna-Maria; Castiglioni, Emiliano; Contini, Stefania; Degiorgis, Fabio; Di Felice, Pina; Donati, Daniele; Fazzolari, Elettra; Gentile, Gabriella; Marchionni, Chiara; Marchioro, Carla; Messina, Flavia; Micheli, Fabrizio; Oliosi, Beatrice; Pavone, Francesca; Pasquarello, Alessandra; Perini, Benedetta; Rinaldi, Marilisa; Sabbatini, Fabio M.; Vitulli, Giovanni; Zarantonello, Paola; Di Fabio, Romano; **St-Denis, Yves**
CORPORATE SOURCE: Psychiatry CEDD, GlaxoSmithKline Medicines Center, Verona, 37135, Italy
SOURCE: ChemMedChem (2007), 2(4), 528-540
CODEN: CHEMGX; ISSN: 1860-7179
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Two new classes of potent and selective CRF1 receptor antagonists, analogs of CP-154,526 (I), are presented. Exploration of general templates based on I through modifications of the top amine and bottom Ph substituents led to optimization of the in vitro affinity and pharmacokinetic profiles. The typical alkyl chains present in the top region of CRF1 antagonists were replaced by substituted heteroaryl moieties, leading to a dramatic improvement of the metabolic stability. This improvement was apparent when the compds. were dosed in vivo: several compds. exhibited low plasma clearance, good oral bioavailability, and high brain penetration. As a consequence of their outstanding pharmacokinetic profiles, these CRF1 antagonists, as exemplified by compound 4 fi (4-(4-bromo-3-methyl-1H-pyrazol- 1-yl)-7-(2,4-dichlorophenyl)-2-methyl-6,7-dihydro-5H-pyrrolo[2,3- d]pyrimidine), produced a dose-dependent "anxiolytic-like" effect when administered orally, decreasing the vocalization of rat pups.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:927207 HCAPLUS Full-text
DOCUMENT NUMBER: 141:395557
TITLE: Preparation of condensed heterocycles as CRF receptor antagonists for treatment of depression, anxiety, IBS, and IBD
INVENTOR(S): Andreotti, Daniele; Bernasconi, Giovanni; Castiglioni, Emiliano; Contini, Stefania; Di Fabio, Romano; Fazzolari, Elettra; Feriani, Aldo; Gentile, Gabriella; Mattioli, Mario; Mingardi, Anna; Sabbatini, Fabio; **St.-Denis, Yves**
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., USA; Neurocrine Biosciences Inc.
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094420	A1	20041104	WO 2004-IB1350	20040407

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004232551	A1	20041104	AU 2004-232551		20040407
CA 2521929	A1	20041104	CA 2004-2521929		20040407
EP 1611133	A1	20060104	EP 2004-726237		20040407
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BR 2004009117	A	20060328	BR 2004-9117		20040407
CN 1805958	A	20060719	CN 2004-80016189		20040407
JP 2006522799	T	20061005	JP 2006-506558		20040407
IN 2005DN04455	A	20070831	IN 2005-DN4455		20051003
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NO 2005005238	A	20060109	NO 2005-5238		20051108
US 2007004708	A1	20070104	US 2006-552493		20060921
PRIORITY APPLN. INFO.:			GB 2003-8208	A	20030409
			US 2003-485322P	P	20030707
			WO 2004-IB1350	W	20040407

OTHER SOURCE(S): MARPAT 141:395557
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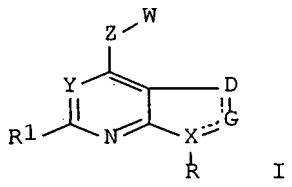

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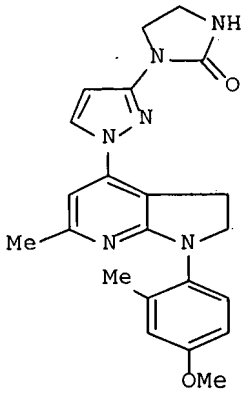


II

AB Title [(pyrrolo[2,3-b]pyridinyl)pyrazolyl]imidazolidinones and related compds. I [wherein D = CR8R9, CR8; G = CR10R11, CR10; W = (un)substituted carbocyclyl, heterocyclyl; X = C, N; Y = N, CR7; Z = (un)substituted heterocyclyl, Ph; R = (un)substituted (hetero)aryl; R1 = H, (cyclo)alkyl, (halo)alkoxy, alkylthio, alkenyl, alkynyl, halo(alkyl), halo, NR3R4, CN; R3, R4 = independently H, alkyl; R7 = H, (halo)alkyl, halo; R8-R11 = independently H, (cyclo)alkyl, alkenyl, alkynyl, NR3R4, CN; and stereoisomers, prodrugs and pharmaceutically acceptable salts, or solvates thereof] were prepared as corticotropin-releasing factor (CRF) antagonists. For example, 4-iodo-6-methyl-1-[2-methyl-

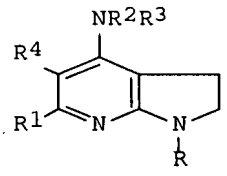
4-(methyloxy)phenyl]-2,3-dihydro- 1H-pyrrolo[2,3-b]pyridine was coupled with 1-(1H-pyrazol-3-yl)imidazolidin- 2-one (preparation of reactants given) in the presence of CuI, K2CO3, dodecane, and trans-cyclohexanediamine in anh. NMP to afford II (53%). In binding assays using recombinant human CRF1 and CRF2 receptors expressed in CHO cell membranes, compds. of the invention showed affinity for CRF receptors with Ki values of <10 μM. Thus, I and their pharmaceutical compns. are useful for the treatment of depression, anxiety, IBS, and IBD (no data).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

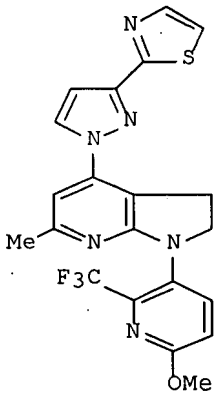
L22 ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:610082 HCAPLUS Full-text
DOCUMENT NUMBER: 141:157105
TITLE: Preparation of heteroaryl-substituted pyrrolo[2,3-b]pyridine derivatives as CRF receptor antagonists
INVENTOR(S): Castiglioni, Emiliano; Di Fabio, Romano; Feriani, Aldo; Micheli, Fabrizio; Sabbatini, Fabio; **St-Denis, Yves**
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., USA; Neurocrine Biosciences Inc.; Glaxo Group Limited
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004062665	A1	20040729	WO 2004-EP409		20040114
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ					
EP 1583531	A1	20051012	EP 2004-701955		20040114
EP 1583531	B1	20070418			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2006515334	T	20060525	JP 2006-500001		20040114
AT 359782	T	20070515	AT 2004-701955		20040114
US 2007066640	A1	20070322	US 2006-542196		20060303
PRIORITY APPLN. INFO.:			US 2003-440432P	P	20030116
			WO 2004-EP409	W	20040114

OTHER SOURCE(S): MARPAT 141:157105
GI



I



II

AB Pyrrolo[2,3-b]pyridines of formula I [R = aryl, heteroaryl; R1 = H, cycloalkyl, alkyl, alkoxy, CN, etc.; NR2R3 = (substituted) aromatic heterocycle; R4 = H, alkyl, halo, haloalkyl] are described, including stereoisomers, prodrugs and pharmaceutically acceptable salts or solvates thereof, processes for their preparation, pharmaceutical compns. containing them and their use in the treatment of conditions mediated by corticotropin-releasing factor (CRF). Thus, II was prepared in several steps.

L22 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:76780 HCAPLUS Full-text
DOCUMENT NUMBER: 138:137174
TITLE: Preparation of triaza- acenaphthylenes and phenalenes as CRF receptor antagonists
INVENTOR(S): Di Fabio, Romano; Micheli, Fabrizio; Regan, Collin F.; Schwaebe, Michael K.; **St-denis, Yves**
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico, Inc., P. R.; Neurocrine Biosciences, Inc.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008414	A1	20030130	WO 2002-US22394	20020715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2452009	A1	20030130	CA 2002-2452009	20020715
AU 2002354916	A1	20030303	AU 2002-354916	20020715

EP 1425281	A1	20040609	EP 2002-752340	20020715
EP 1425281	B1	20060201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011220	A	20040713	BR 2002-11220	20020715
CN 1541217	A	20041027	CN 2002-815746	20020715
JP 2004537555	T	20041216	JP 2003-513973	20020715
HU 2004000460	A2	20050128	HU 2004-460	20020715
NZ 530508	A	20051125	NZ 2002-530508	20020715
AT 316972	T	20060215	AT 2002-752340	20020715
ES 2256506	T3	20060716	ES 2002-2752340	20020715
ZA 2003009942	A	20040525	ZA 2003-9942	20031223
IN 2003DN02291	A	20060120	IN 2003-DN2291	20031230
NO 2004000203	A	20040316	NO 2004-203	20040116
MX 2004PA00492	A	20050307	MX 2004-PA492	20040116
US 2004242623	A1	20041202	US 2004-483872	20040729
US 7273871	B2	20070925		
PRIORITY APPLN. INFO.:			GB 2001-17395 A	20010717
			WO 2002-US22394 W	20020715

OTHER SOURCE(S): MARPAT 138:137174
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Triaza- acenaphthylenes and phenalenes [e.g., I; wherein R = (substituted) aryl, heteroaryl; R1 = H, (C1-C6)alkyl, (C2-C6)alkenyl, (C2-C6)alkynyl, halo(C1-C6)alkyl, halo(C1-C6)alkoxy, NH2, CN; R2 = H, alkyl, ether, thioether, amine; R3 = H, (C2-C6)alkenyl, (C2-C6)alkynyl, etc.; R4 = H, (C1-C6)alkyl, halo, halo(C1-C6)alkyl; Y = C, N; m, n, independently = 0, 1] were prepared For example, compound (II) was prepared by the provided method. The prepared compds. are useful in the treatment of conditions mediated by corticotropin-releasing factor (CRF) (no data).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:76778 HCAPLUS Full-text
DOCUMENT NUMBER: 138:137173
TITLE: Preparation of pyrazolyl- pyrrolo[2,3-b]pyridines and tetrahydro[1,8]naphthyridines as CRF receptor antagonists
INVENTOR(S): Di Fabio, Romano; Micheli, Fabrizio; **St-denis, Yves**
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008412	A2	20030130	WO 2002-EP7865	20020715
WO 2003008412	A3	20030501		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

GB 2378702	A	20030219	GB 2002-16041	20020711
CA 2451530	A1	20030130	CA 2002-2451530	20020715
AU 2002328899	A1	20030303	AU 2002-328899	20020715
EP 1425280	A2	20040609	EP 2002-764696	20020715
EP 1425280	B1	20060830		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011171	A	20040810	BR 2002-11171	20020715
CN 1525972	A	20040901	CN 2002-813866	20020715
HU 2004000465	A2	20050128	HU 2004-465	20020715
JP 2005514328	T	20050519	JP 2003-513971	20020715
NZ 530043	A	20060331	NZ 2002-530043	20020715
EP 1695974	A1	20060830	EP 2006-76176	20020715
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
AT 338042	T	20060915	AT 2002-764696	20020715
ES 2271327	T3	20070416	ES 2002-2764696	20020715
IN 2003DN02137	A	20070302	IN 2003-DN2137	20031209
ZA 2003009708	A	20050121	ZA 2003-9708	20031215
US 2004171607	A1	20040902	US 2004-483792	20040114
US 7253284	B2	20070807		
NO 2004000206	A	20040316	NO 2004-206	20040116
MX 2004PA00494	A	20040504	MX 2004-PA494	20040116
HK 1066535	A1	20070309	HK 2004-109443	20041130
US 2007219232	A1	20070920	US 2007-749433	20070516
PRIORITY APPLN. INFO.:			GB 2001-17396	A 20010717
			EP 2002-764696	A3 20020715
			WO 2002-EP7865	W 20020715
			US 2004-483792	A1 20040114

OTHER SOURCE(S): MARPAT 138:137173
GI

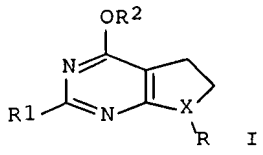
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Pyrazolyl- pyrrolo[2,3-b]pyridines and tetrahydro[1,8]naphthyridines [I; wherein R = (substituted) aryl, heteroaryl; R1 = H, (C1-C6)alkyl, (C2-C6)alkenyl, (C2-C6)alkynyl, halo(C1-C6)alkyl, halo(C1-C6)alkoxy, halogen, amino, or cyano; R2 = H, (C3-C7)cycloalkyl; R3 = (C3-C7)cycloalkyl; or R2 and R3 together with N form a (substituted) 5-14 membered heterocycle; R4 = H, (C1-C6)alkyl, halo, halo(C1-C6)alkyl; X = C, N; n = 1 or 2] were prepared For example, compound (II) was prepared by the provided method. The prepared compds. are useful in the treatment of conditions mediated by corticotropin-releasing factor (CRF) (no data).

L22 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:964359 HCAPLUS Full-text
DOCUMENT NUMBER: 138:39290
TITLE: Preparation of substituted 6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidines as corticotropin releasing factor antagonists
INVENTOR(S): Di Fabio, Romano; Marchionni, Chiara; Micheli, Fabrizio; Pasquarello, Alessandra; Perini, Benedetta; **St-Denis, Yves**
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002100863	A1	20021219	WO 2002-GB2656		20020611
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002302807	A1	20021223	AU 2002-302807		20020611
EP 1395591	A1	20040310	EP 2002-730487		20020611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004533465	T	20041104	JP 2003-503630		20020611
US 2005054661	A1	20050310	US 2004-480958		20041103
PRIORITY APPLN. INFO.:			GB 2001-14343	A	20010612
			GB 2001-14349	A	20010612
			GB 2001-17399	A	20010717
			WO 2002-GB2656	W	20020611

OTHER SOURCE(S): MARPAT 138:39290
GI



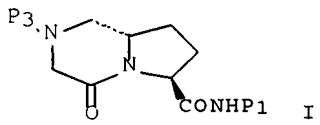
I

AB The title compds. [I; R = (un)substituted aryl, heteroaryl; R1 = H, alkyl, alkenyl, alkynyl, etc.; R2 = CHR6R7; R3, R4 = H, alkyl; R5 = (un)substituted aryl, 5-6 membered heterocycle or cycloalkyl, which may contain one or more double bonds; aryl; R6, R7 = H, (un)substituted alkenyl, alkyl; X = C, N],

useful in the treatment of conditions mediated by corticotropin-releasing factor (CRF) such as depression and anxiety, were prepared Thus, reacting 3-pentanol with 4-chloro-7-(2,4- dichlorophenyl)-2-methyl-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidine (preparation given) in the presence of NaH in DMF afforded I [R = 2,4-Cl2C6H4; R1 = Me; R2 = OCHEt2; X = N] which showed Ki of < 0.1 μM against CRF receptor binding. Use of radiolabeled compds. I in the diagnostic methods of conditions mediated by CRF was claimed.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:251344 HCAPLUS Full-text
DOCUMENT NUMBER: 137:332728
TITLE: Novel bicyclic lactam inhibitors of thrombin: highly potent and selective inhibitors
AUTHOR(S): **St-Denis, Yves**; Levesque, Sophie; Bachand, Benoit; Edmunds, Jeremy J.; Leblond, Lorraine; Preville, Patrice; Tarazi, Micheline; Winocour, Peter D.; Siddiqui, M. Arshad
CORPORATE SOURCE: Shire BioChem., Laval, QC, H7V 4A7, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(8), 1181-1184
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:332728
GI



I

AB The potency and selectivity of a previous series of low mol. weight thrombin inhibitors were improved through modifications of the P1 and P3 residues in the formula I. Introduction of di-Ph substituted sulfonamides in the P3 moiety led to highly efficacious compds. By correctly selecting the combination of P1 and P3 residues, high levels of potency, selectivity and in vivo efficacy were obtained.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:872229 HCAPLUS Full-text
DOCUMENT NUMBER: 136:210039
TITLE: Novel bicyclic lactam inhibitors of thrombin: potency and selectivity optimization through P1 residues
AUTHOR(S): Levesque, Sophie; **St. Denis, Yves**; Bachand, Benoit; Preville, Patrice; Leblond, Lorraine; Winocour, Peter D.; Edmunds, Jeremy J.; Rubin, J. R.; Siddiqui, M. Arshad
CORPORATE SOURCE: Shire BioChem Inc., Laval, QC, H7V 4A7, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001),

11(24), 3161-3164
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:210039
AB Peptidomimetic inhibitors of thrombin lacking the important Ser195-carbonyl interaction have been prepared The binding energy lost after the removal of the activated carbonyl was recaptured through a series of modifications of the P1 residues of the bicyclic lactam inhibitors. Selected substituted compds. displayed useful pharmacol. profiles both in vitro and in vivo.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 10 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:265403 HCAPLUS Full-text
DOCUMENT NUMBER: 134:295839
TITLE: Preparation of 2-phenylpiperazine-1-carboxylic acid benzylamides as tachykinin antagonists
INVENTOR(S): Alvaro, Giuseppe; Di Fabio, Romano; Giovannini, Riccardo; Guercio, Giuseppe; **St. Denis, Yves** ; Ursini, Antonella
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001025219	A2	20010412	WO 2000-EP9722	20001005
WO 2001025219	A3	20011213		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2386515	A1	20010412	CA 2000-2386515	20001005
EP 1218359	A2	20020703	EP 2000-969414	20001005
EP 1218359	B1	20040707		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
TR 200200936	T2	20020722	TR 2002-936	20001005
BR 2000014541	A	20020917	BR 2000-14541	20001005
HU 200203136	A2	20030228	HU 2002-3136	20001005
JP 2003511377	T	20030325	JP 2001-528165	20001005
AU 768780	B2	20040108	AU 2000-79139	20001005
NZ 518144	A	20040430	NZ 2000-518144	20001005
AT 270664	T	20040715	AT 2000-969414	20001005
EP 1454901	A1	20040908	EP 2004-76650	20001005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, CY				

EP 1460066	A1	20040922	EP 2004-76632	20001005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, CY				
PT 1218359	T	20041029	PT 2000-969414	20001005
ES 2222927	T3	20050216	ES 2000-969414	20001005
NZ 531127	A	20051125	NZ 2000-531127	20001005
TW 225485	B	20041221	TW 2000-89121014	20001007
ZA 2002002589	A	20030703	ZA 2002-2589	20020403
IN 2002MN00412	A	20050318	IN 2002-MN412	20020404
NO 2002001637	A	20020606	NO 2002-1637	20020405
NO 323776	B1	20070702		
MX 2002PA03515	A	20020902	MX 2002-PA3515	20020405
US 6951861	B1	20051004	US 2002-89964	20020508
US 2003028021	A1	20030206	US 2002-190170	20020703
US 6642240	B2	20031104		
US 2004048862	A1	20040311	US 2003-637825	20030808
US 7071196	B2	20060704		
AU 2004201361	A1	20040429	AU 2004-201361	20040331
AU 2004201361	B2	20070906		
US 2004209893	A1	20041021	US 2004-838838	20040504
US 2006122192	A1	20060608	US 2006-334267	20060118

PRIORITY APPLN. INFO.:	GB 1999-23748	A	19991007
	AU 2000-79139	A	20001005
	EP 2000-969414	A3	20001005
	WO 2000-EP9722	W	20001005
	US 2002-89964	A1	20020508
	US 2002-190170	A1	20020703
	US 2003-637825	A1	20030808

OTHER SOURCE(S): MARPAT 134:295839
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to piperazine derivs. I [wherein: R = halo, C1-4 alkyl; R1 = H, C1-4 alkyl; R2 = H, C1-4 alkyl, C2-6 alkenyl, C3-7 cycloalkyl; or NR1CR2 = 5- to 6-membered heterocyclyl; R3 = CF3, C1-4 alkyl, C1-4 alkoxy, CF3O, or halo; R4 = H, (CH2)qR7 or (CH2)rCO(CH2)pR7; R5 = H, C1-4 alkyl or COR6; R6 = H, OH, NH2, NHMe, NMe2, 5-membered heteroaryl containing 1-3 N/O/S or 6-membered heteroaryl containing 1-3 N atoms; R7 = H, OH, or NR8R9 wherein R8 and R9 = H or C1-4 alkyl (un)substituted by OH or by NH2; R10 = H, C1-4 alkyl; or R10 and R2 form C3-7 cycloalkyl; m, n = 0-3; p, r = 0-4; q = 1-4; provided that, when NR1CR2 = 5- to 6-membered heterocyclic, then (i) m = 1 or 2; (ii) when m = 1, R ≠ F; and (iii) when m = 2, both R ≠ F] and pharmaceutically acceptable salts and solvates thereof. The compds. are potent and specific antagonists of tachykinins, including substance P and other neurokinins. Examples include 38 syntheses, 82 prepns. of intermediates, 4 standard formulations, and 2 bioassays. For instance, (+)-(S)-3-(4-fluoro-2- methylphenyl)piperazin-2-one (preparation given) was treated with triphosgene and amidated with 3,5-(F3C)2C6H3CHMeNHMe to give 2 diastereomeric amides. Separation of the (S,S)-diastereomer by flash chromatog. and reduction of the ring oxo group with BH3.THF gave title compound II, isolated as the acetate salt (III). Using the gerbil foot-tapping model for reversal of an NK1 agonist, III had an oral ED50 of 0.04 mg/kg.

L22 ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:118603 HCAPLUS Full-text
DOCUMENT NUMBER: 134:326510
TITLE: Potent and selective bicyclic lactam inhibitors of thrombin. Part 4: transition state inhibitors
AUTHOR(S): Bachand, B.; Tarazi, M.; **St. Denis, Y.**; Edmunds, J. J.; Winocour, P. D.; Leblond, L.; Siddiqui, M. A.
CORPORATE SOURCE: BioChem Pharma Inc., Laval, QC, H7V 4A7, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(3), 287-290
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:326510
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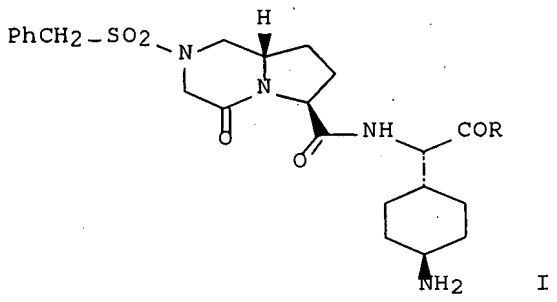

I

AB Title compds. I (R = 2-thiazolyl, 2-benzothiazolyl, CONHMe, CO2Me, CO2H, CO2Bu, COSEt, CONHCH2CO2H, 1-methyltetrazolyl, etc.) were prepared as thrombin inhibitors and were evaluated in vitro and in vivo. I, having in common an electrophilic basic trans-cyclohexylamine P1 residue, displayed high thrombin affinity, high selectivity against trypsin and good in vivo efficacy in the rat arterial thrombosis model.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:525214 HCAPLUS Full-text
DOCUMENT NUMBER: 133:252587
TITLE: Synthesis of 8-epi-castanospermine and 6,7,8-tri-epi-castanospermine
AUTHOR(S): **St. Denis, Yves**; Chan, Tak Hang
CORPORATE SOURCE: Department of Chemistry, McGill University, Montreal, QC, H3A 2K6, Can.
SOURCE: Canadian Journal of Chemistry (2000), 78(6), 776-783
CODEN: CJCHAG; ISSN: 0008-4042
PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:252587

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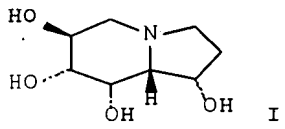

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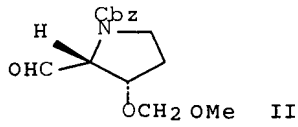

II

AB 8-Epi-Castanospermine (I) and 6,7,8-tri-epi-castanospermine were synthesized from the hydroxyproline precursor II which was obtained enantioselectively via an enzymic process.

L22 ANSWER 13 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:60208 HCAPLUS Full-text
DOCUMENT NUMBER: 132:245827
TITLE: Structural Basis of the Thrombin Selectivity of a Ligand That Contains the Constrained Arginine Mimic (2S)-2-Amino-(3S)-3-(1-carbamimidoyl-piperidin-3-yl)-propanoic Acid at P1
AUTHOR(S): Narasimhan, Lakshmi S.; Rubin, J. Ronald; Holland, Debra R.; Plummer, Janet S.; Rapundalo, Stephen T.; Edmunds, Jeremy E.; **St. Denis, Yves**; Siddiqui, M. Arshad; Humblet, Christine
CORPORATE SOURCE: Parke-Davis Pharmaceutical Research Division of Warner-Lambert Company, Ann Arbor, MI, 48105, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(3), 361-368
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have studied the thrombin and trypsin complexed structures of a pair of peptidomimetic thrombin inhibitors, containing different P1 fragments. The first has arginine as its P1 fragment, and the second contains the constrained arginine mimic (2S)-2-amino-(3S)-3-(1-carbamimidoyl-piperidin- 3-yl)-propanoic acid (SAPA), a fragment known to enhance thrombin/trypsin selectivity of inhibitors. On the basis of an anal. of the nonbonded interactions present in the structures of the trypsin and thrombin complexes of the two inhibitors, the calculated accessible surfaces of the enzymes and inhibitors in the four complexes, data on known structures of trypsin complexes of inhibitors, and factor Xa inhibitory potency of these compds., we conclude that the ability of this arginine mimic to increase thrombin selectivity of an inhibitor is mediated by its differential interaction with the residue at position 192 (chymotrypsinogen numbering). Thrombin has a glutamic acid at residue 192, and trypsin has a glutamine. The anal. also suggests that this constrained arginine mimic, when present in an inhibitor, might enhance selectivity against other trypsin-like enzymes that have a glutamine at residue position 192.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 14 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:761523 HCAPLUS Full-text
DOCUMENT NUMBER: 132:12502
TITLE: Preparation of substituted purinyl derivatives with

immunomodulating activity

INVENTOR(S): Penney, Christopher; Zacharie, Boulos; Gagnon, Lyne; Attardo, Giorgio; Connolly, Timothy P.; **St. Denis, Yves**; Kadhim, Salam

PATENT ASSIGNEE(S): Biochem Pharma, Can.

SOURCE: U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 264,028, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5994361	A	19991130	US 1995-474073	19950607
CA 2165956	A1	19951228	CA 1995-2165956	19950621
ZA 9505131	A	19970324	ZA 1995-5131	19950621
CN 1157618	A	19970820	CN 1995-194679	19950621
CN 1051083	B	20000405		
HU 77780	A2	19980828	HU 1996-3492	19950621
AU 9523200	A	19960111	AU 1995-23200	19950622
AU 9863678	A	19980618	AU 1998-63678	19980428
AU 717160	B2	20000316		

PRIORITY APPLN. INFO.:

US 1994-264028	B2	19940622
US 1995-474073	A	19950607
US 1995-487329	A	19950607

OTHER SOURCE(S): MARPAT 132:12502

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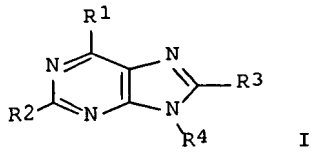

I

AB Purinyl derivs. I [R1 is substituted amino represented by NR5R6, where R5 and R6 are H, alkyl, unsubstituted amino (R5 and R6 are not both H or amino); R2, R3 = H, alkyl, amino, (un)substituted thiol; halo; R4 = R12-X12, where R12 is a saturated or unsatd. linear hydrocarbon chain of 5-20 carbons optionally containing one or more interruptions within the chain by a heteroatom and optionally substituted with one or more :O, or :S and X12 is hydroxy, an aminoalkyl group, or a known amino acid bound by its α-amino group] were prepared as immunomodulating agents. Thus, N-[[5-[6-(dimethylamino)purin-9-yl]pentoxy]carbonyl]-D-arginine was prepared and in combination with 5FU (50 and 20 mg/kg, resp.) showed a markedly higher antitumor activity than 5FU + levamisole.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 15 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:614098 HCAPLUS Full-text

DOCUMENT NUMBER: 132:3352

TITLE: The design of potent and selective inhibitors of

thrombin utilizing a piperazinedione template. Part 1

AUTHOR(S): Cody, Wayne L.; Cai, Cuiman; Doherty, Annette M.; Edmunds, Jeremy J.; He, John X.; Narasimhan, Lakshmi S.; Plummer, Janet S.; Rapundalo, Stephen T.; Rubin, J. Ronald; Van Huis, Chad A.; **St. Denis, Yves**; Winocour, Peter D.; Siddiqui, M. Arshad

CORPORATE SOURCE: Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, MI, 48105, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(17), 2497-2502
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

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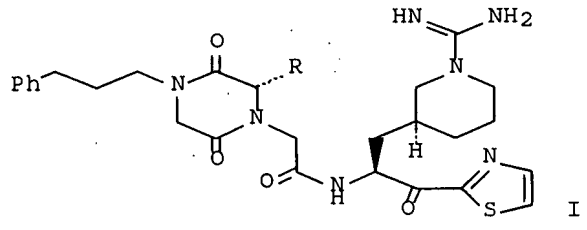

I

AB Utilizing X-ray crystallog. and mol. modeling, highly potent and selective peptidomimetic thrombin inhibitors have been designed containing a rigid piperazinedione template, I (R = CH2Ph, H, 3-pyridylmethyl, etc.). The synthesis and biol. activity of these compds. is described. The replacement of the benzyl group with aliphatic moieties led to compds. with reasonable selectivity for thrombin over trypsin. All of the compds. were relatively weak inhibitors. I [R = CH2(C6H11)] was the most potent among them.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:275284 HCAPLUS Full-text

DOCUMENT NUMBER: 131:53581

TITLE: Potent and selective bicyclic lactam inhibitors of thrombin: Part 3: P1' modifications

AUTHOR(S): Plummer, Janet S.; Berryman, Kent A.; Cai, Cuiman; Cody, Wayne L.; DiMaio, John; Doherty, Annette M.; Eaton, Scott; Edmunds, Jeremy J.; Holland, Debra R.; Lafleur, D.; Levesque, Sophie; Narasimhan, Lakshmi S.; Rubin, J. Ronald; Rapundalo, Stephen T.; Siddiqui, M. Arshad; Susser, A.; **St. Denis, Yves**; Winocour, Peter

CORPORATE SOURCE: Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, MI, 48105, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(6), 835-840
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthesis and antithrombotic activity of a series of nonpeptide bicyclic thrombin inhibitors are described. We have explored the SAR around the P1' site. Modification of the P1' site has been found to affect potency and selectivity.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 17 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:92591 HCAPLUS Full-text
TITLE: The discovery of potent and selective peptidomimetic inhibitors of thrombin
AUTHOR(S): Cody, W. L.; Berryman, K. A.; Cai, C.; Doherty, A. M.; Edmunds, J. J.; He, J. X.; Holland, D. R.; Narasimhan, L.; Plummer, J. S.; Rapundalo, S. T.; Susser, A.; VanHuis, C. A.; Siddiqui, M. A.; **St-Denis, Y.**
CORPORATE SOURCE: Departments of Chemistry, Parke-Davis Pharmaceutical Research, Warner-Lambert Co., Ann Arbor, MI, 48105, USA
SOURCE: Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), MEDI-077. American Chemical Society: Washington, D. C.
CODEN: 67GHA6
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB We have utilized X-ray crystallog. and mol. modeling in a structure based design approach to develop highly potent and selective peptidomimetic thrombin inhibitors from the peptidic inhibitor, DPhe-Pro-Arg-CMK. In particular, a suitably functionalized rigid monocyclic template resulted in inhibitors with low nanomolar affinity. In addition, the incorporation of arginine mimetics led to thrombin selectivity. For example, PD 180849 possessed IC50's of 18 and 9700 nM for thrombin and trypsin, resp. The discovery of PD 180849 and the mol. interactions providing the selectivity will be described.

L22 ANSWER 18 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:1273 HCAPLUS Full-text
DOCUMENT NUMBER: 130:191421
TITLE: Potent bicyclic lactam inhibitors of thrombin: Part I: P3 modifications
AUTHOR(S): **St. Denis, Yves**; Augelli-Szafran, Corinne E.; Bachand, Benoit; Berryman, Kent A.; DiMaio, John; Doherty, Annette M.; Edmunds, Jeremy J.; Leblond, Lorraine; Levesque, Sophie; Narasimhan, Lakshmi S.; Penvose-Yi, Jan R.; Rubin, J. Ronald; Tarazi, Micheline; Winocour, Peter D.; Siddiqui, M. Arshad
CORPORATE SOURCE: BioChem Therapeutic Inc., Laval, QC, H7V 4A7, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(22), 3193-3198
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
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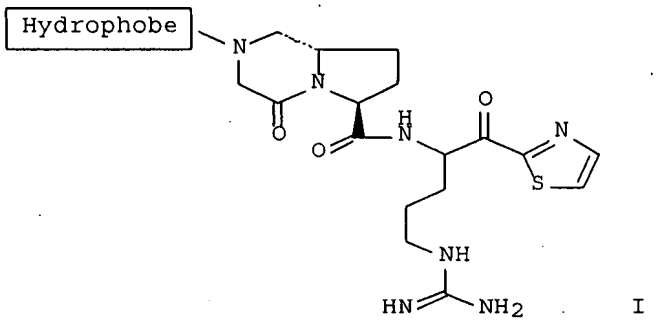

I

AB Peptidomimetic inhibitors of general structure (I) have been prepared Optimization of the binding affinities of these compds. through variation of the P3 hydrophobic residue is described. Selected substituted bicyclic lactams displayed interesting pharmacol. profiles both in vitro and in vivo.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 19 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:812466 HCAPLUS Full-text

DOCUMENT NUMBER: 130:125372

TITLE: Potent and selective bicyclic lactam inhibitors of thrombin: part 2: P1 modifications

AUTHOR(S): Plummer, Janet S.; Berryman, Kent A.; Cai, Cuiman; Cody, Wayne L.; DiMaio, John; Doherty, Annette M.; Edmunds, Jeremy J.; He, John X.; Holland, Debra R.; Levesque, Sophie; Kent, Darin R.; Narasimhan, Lakshmi S.; Rubin, J. Ronald; Rapundalo, Stephen T.; Siddiqui, M. Arshad; Susser, Alan J.; **St. Denis, Yves**; Winocourt, Peter D.

CORPORATE SOURCE: Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, MI, 48105, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(23), 3409-3414
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

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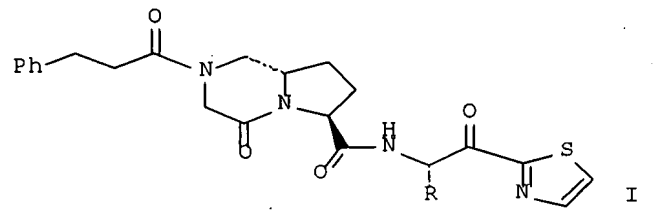

I

AB The synthesis and antithrombotic activity of a series of thrombin inhibitors, which are octahydropyrrolpyrazine-based, bicyclic lactams I (R = 3-guanidinopropyl, 3-amidinobenzyl, 1-amidino-3-piperidinylmethyl, 4-aminocyclohexyl, 1-amidino-4-piperidinyl), are described. The authors have explored the structure-activity relationships with modifications to the P1 site. The introduction of arginine mimetics at the PI site led to potent and selective thrombin inhibitors.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 20 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:220857 HCAPLUS Full-text
DOCUMENT NUMBER: 128:308700
TITLE: Preparation of heteronaphthoquinone glycosides as antitumors
INVENTOR(S): Attardo, Giorgio; Breining, Tibor; Courchesne, Marc; Lamothe, Serge; Lavallee, Jean-Francedillaois; Nguyen, Dieu; Rej, Rabindra; **St. Denis, Yves**; Wang, Wuyi; Xu, Yao-Chang; Barbeau, France; Lebeau, Elaine; Kraus, Jean Louis
PATENT ASSIGNEE(S): Biochem Pharma Inc., Can.
SOURCE: U.S., 153 pp., Cont.-in-part of U.S. Ser. No. 148,251, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5736523	A	19980407	US 1995-401493	19950310
PRIORITY APPLN. INFO.:			US 1992-973233 B2	19921109
			US 1993-148251 B2	19931105

OTHER SOURCE(S): MARPAT 128:308700
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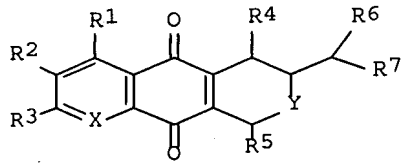


I

AB Naphthoquinone glycosides I (R1-R3 ,Q = H, OH, CN, NO2, alkyl, alkenyl, alkynyl, alkoxy, aryl, aralkyl, aryloxy, alkoxyalkyl, acyl, amine, amido, sulfono, acyloxy, halo; R4 = H, OH, alkyl, alkoxy, acyl, amino, amido, sulfono, ester, phosphono, halo, morpholino; R5 = H, OH, alkyl, alkoxy, acyl, amino, amido, sulfono, ester, phosphono, halo, morpholino, sugar; R6, R7 = H, CN, NO2, alkyl, alkenyl, alkynyl, alkoxy, aralkyl, aryloxy, acyl, amine, sulfono, ester, phosphono, halo; X = N, NO, CQ; Y = O, S SO2) were prepared as antitumor agents in mammals. Thus, (1'S,1S,3R)-Me (5,10,dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L- lyxohexopyranose)-3,4,5,10-

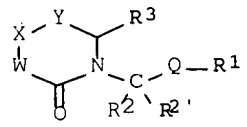
tetrahydronaphtho[2,3-C]pyran-3-yl)ketone (II) was prepared as antitumor agent. In breast cancer, II is less potent than adriamycin but nearly as effective in the sensitive and adriamycin resistant cell line.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 21 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:175945 HCAPLUS Full-text
DOCUMENT NUMBER: 128:244342
TITLE: Preparation of lactam inhibitors of thrombin
INVENTOR(S): **St. Denis, Yves**; Siddiqui, M. Arshad; Cody, Wayne Livingston; Edmunds, Jeremy John; Plummer, Janet Samartino
PATENT ASSIGNEE(S): Biochem Pharma, Inc., Can.
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809987	A1	19980312	WO 1997-US15312	19970905
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9741723	A	19980326	AU 1997-41723	19970905
PRIORITY APPLN. INFO.:			GB 1996-18687	A 19960906
			US 1996-25599P	P 19960906
			WO 1997-US15312	W 19970905

OTHER SOURCE(S): MARPAT 128:244342
GI

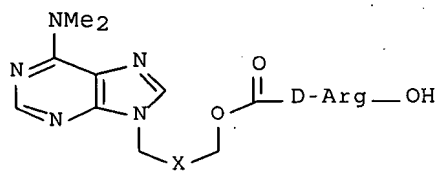


I

AB Heterocyclic thrombin inhibitors I (W, X = CHR4, CR4, NR4, N, O, S, SO, SO2, provided that at least one of W and X is NR4, N, O, S, SO, SO2; Y = CHR4, CR4, CO; Q = CO, CS, CHR4; R1 is a polar amino acid residue or derivative or analog optionally substituted with an amino acid, peptide, or heterocycle; R2, R2' = H, halo, or alkyl optionally substituted by an aryl, heterocyclic or cycloalkyl group; R3, R4 = H, NH2, alkylamino, CO2H, aryl, cycloalkyl, etc.) were prepared Thus, N-[4-guanidino-1-(thiazole-2- carbonyl)butyl]-2-[2-oxo-4-(3-phenylpropionyl)-1-piperazinyl]acetamide, prepared by a coupling procedure in which the guanidino group is protected by 4-methoxy-2,3,6-trimethylbenzenesulfonyl, was assayed for thrombin affinity (IC50 = 35 nM).

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 22 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:526712 HCAPLUS Full-text
DOCUMENT NUMBER: 127:191025
TITLE: Synthesis and Activity of 6-Substituted Purine Linker Amino Acid Immunostimulants
AUTHOR(S): Zacharie, Boulos; Gagnon, Lyne; Attardo, Giorgio; Connolly, Timothy P.; **St. Denis, Yves**; Penney, Christopher L.
CORPORATE SOURCE: Department of Medicinal Chemistry, BioChem Therapeutic Inc., Laval, QC, H7V 4A7, Can.
SOURCE: Journal of Medicinal Chemistry (1997), 40(18), 2883-2894
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A series of 6-substituted purinyl alkoxycarbonyl amino acids, e.g. I (X = divalent linker group) were synthesized and evaluated for their ability to stimulate cytotoxic T lymphocytes (CTLs) and the mixed lymphocyte reaction (MLR). A few of these compds., in particular I [X = (CH2)3] (BCH-1393), displayed an in vitro stimulation of CTLs comparable to interleukin 2 (IL 2). BCH-1393 increased the CTL response between 10-9 M and 10-5 M. Further, this potent in vitro activity was reflected as a significant increase in CTL cell number in vivo. However, immunophenotyping of some of the other equipotent compds. did not reveal a parallel relative increase in CTLs in vivo. It was difficult to formulate a rigorous structure-activity relationship based on in vitro CTL activity. Nevertheless, the activity was dependent upon the nature of the 6-substituent on the purine, the type and stereochem. of the amino acid, and the distance and spatial freedom between the purine and amino acid as defined by the length and rigidity of the linker. These compds. were generally nontoxic, as exemplified by BCH-1393. BCH-1393 is a promising immunostimulant which may be targeted for those disease states which require an increased CTL or TH1 type response.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

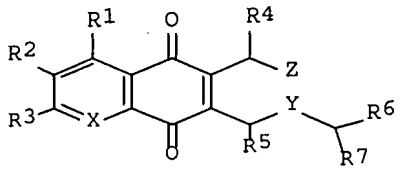
L22 ANSWER 23 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:169186 HCAPLUS Full-text
DOCUMENT NUMBER: 126:251355
TITLE: Preparation of heteronaphthoquinone glycosides as antitumors
INVENTOR(S): Attardo, Giorgio; Breining, Tibor; Courchesne, Marc;

Lamothe, Serge; Lavallee, Jean Francois; Nguyen, Dieu; Rej, Rabindra; **St. Denis, Yves**; Wang, Wuyi; Xu, Yao Chang; Barbeau, France; Lebeau, Elaine; Kraus, Jean L.

PATENT ASSIGNEE(S): Biochem Pharma Inc., Can.
SOURCE: U.S., 162 pp., Cont.-in-part of U.S. Ser. No. 148,251.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 5606037	A	19970225	US 1995-401492		19950310
PRIORITY APPLN. INFO.:			US 1992-973233	B2	19921109
			US 1993-148251	A2	19931105

OTHER SOURCE(S): MARPAT 126:251355
GI



I

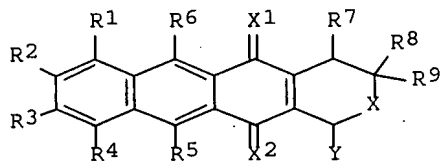
AB Naphthoquinone glycosides I (R1-R3 ,Q = H, OH, CN, NO2, alkyl, alkenyl, alkynyl, alkoxy, aryl, aralkyl, aryloxy, alkoxyalkyl, acyl, amine, amido, sulfono, acyloxy, halo; R4 = H, OH, alkyl, alkoxy, acyl, amino, amido, sulfono, ester, phosphono, halo, morpholino; R5 = H, OH, alkyl, alkoxy, acyl, amino, amido, sulfono, ester, phosphono, halo, morpholino, sugar; R6, R7 = H, CN, NO2, alkyl, alkenyl, alkynyl, alkoxy, aralkyl, aryloxy, acyl, amine, sulfono, ester, phosphono, halo; X = N, NO, CQ; Y = O, S SO2; Z = single or double bond) were prepared as antitumor agents in mammals. Thus, (1'S,1S,3R)methyl (5,10,dioxo-1-(2',3',6'-trideoxy-3'- trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)-3,4,5,10- tetrahydronaphtho[2,3-C]pyran-3-yl)ketone (II) was prepared as antitumor agent. In breast cancer, II is less potent than adriamycin but nearly as effective in the sensitive and adriamycin resistant cell line.

L22 ANSWER 24 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:97726 HCAPLUS Full-text
DOCUMENT NUMBER: 126:199791
TITLE: Preparation of heterocyclic anthracycline glycosides as antitumors
INVENTOR(S): Attardo, Giorgio; Kraus, Jean-Louis; Courchesne, Marc; Lamonthe, Serge; Lavallee, Jean-Francois; Lebeau, Elaine; Nguyen, Dieu; Rej, Rabindra; **St. Denis, Yves**; Wang, Wuyi; Xu, Yao-Chang; Barbeau, France; Bellea, Bernard

PATENT ASSIGNEE(S): Biochem Pharma Inc., Can.
SOURCE: U.S., 191 pp., Cont.-in-part of U.S. Ser. No. 2,766, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5593970	A	19970114	US 1994-263925	19940620
PRIORITY APPLN. INFO.:			US 1990-536107 B2	19900611
			US 1992-859244 B2	19920326
			US 1993-2766 B2	19930113

OTHER SOURCE(S): MARPAT 126:199791
GI



I

AB Novel pyrano heterocyclic anthracycline glycosides I [X1,X2 = O, S, (un)substituted amine; X = O, S, SO, SO2, (un)substituted amine; R1-R6 = H, OH, alkyl, acyl, halogen, silane, sulfonate, ureido , (un)substituted amine; R7 = H, OH, halo, alkyl, CN, NH2, acyloxy, acyl; R8 = H, alkyl, alkoxy, acyl, acyloxy, aryl, aryloxy, squaric acid; R9 = H, halogen, alkyl, alkoxy, (un)substituted amine; Y = saccharide] were prepared as antitumors for treatment of breast cancer, leukemia, lung cancer, colon cancer, ovarian cancer, renal cancer, and melanoma. As well, these compds. may be used ex vivo for the treatment of cancerous bone marrow before retransplanting said marrow in a patient. Pharmaceutical compns. and methods of preparing the compds. are also described. Thus, (1'S,1S,3R)-methyl-(11-hydroxy-6-methoxy-1-[2',3',6'-trideoxy-3- trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose]-5,12-dioxo-3,4,5,12- tetrahydroanthracen[2,3,c]pyran-3-yl)formate was prepared and tested as antitumor (IC50 = 0.91-7.46 μM).

L22 ANSWER 25 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:509465 HCAPLUS Full-text
DOCUMENT NUMBER: 125:167970
TITLE: Low molecular weight bicyclic thrombin inhibitors
INVENTOR(S): Dimaio, John; Siddiqui, M. Arshad; Gillard, John W.; **St-Denis, Yves**; Tarazi, Micheline; Preville, Patrice; Levesque, Sophie; Bachand, Benoit
PATENT ASSIGNEE(S): Biochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 182 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9619483	A1	19960627	WO 1995-CA708		19951221
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2208772	A1	19960627	CA 1995-2208772		19951221
AU 9642505	A	19960710	AU 1996-42505		19951221
EP 802916	A1	19971029	EP 1995-940923		19951221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV					
CN 1175259	A	19980304	CN 1995-197614		19951221
HU 77651	A2	19980728	HU 1998-216		19951221
BR 9510433	A	19981110	BR 1995-10433		19951221
NZ 297360	A	20000327	NZ 1995-297360		19951221
AU 9540628	A	19960704	AU 1995-40628		19951222
AU 715378	B2	20000203			
ZA 9510960	A	19960709	ZA 1995-10960		19951222
ZA 9510961	A	19960709	ZA 1995-10961		19951222
FI 9702466	A	19970819	FI 1997-2466		19970611
NO 9702892	A	19970820	NO 1997-2892		19970620
US 6057314	A	20000502	US 1997-880885		19970623
LV 12019	B	19980720	LV 1997-141		19970715
LT 4368	B	19980825	LT 1997-132		19970721
PRIORITY APPLN. INFO.:			GB 1994-26038	A	19941222
			GB 1995-3136	A	19950217
			GB 1995-10265	A	19950522
			GB 1995-10266	A	19950522
			GB 1995-10267	A	19950522
			WO 1995-CA708	W	19951221
OTHER SOURCE(S):	MARPAT 125:167970				

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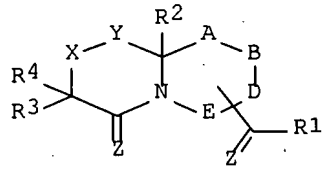

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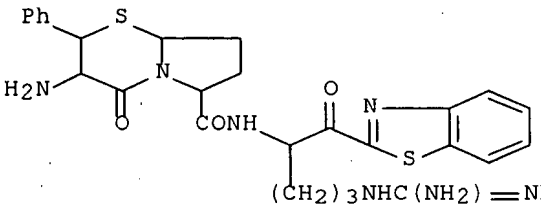

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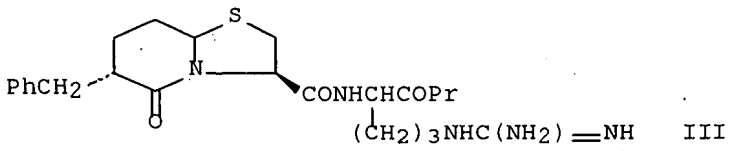

III

AB Heterobicyclic thrombin inhibitors I (A, B = CH, S, O, etc.; D = CH, C-alkyl, etc.; E = CH2, CH-acyl; X = O, NH, etc.; Y = O, S, SO, etc.; Z = O, S, etc.; R1 = e.g., arginyl moiety substituted with an amino acid or heterocycle; R2 = H or organyl; R3 = H, amino, etc.; R4 = H, aryl, cycloalkyl, etc.) were prepared Thus, benzothiazole derivative II was prepared in 7 steps from PhCH2SCH2CH(NHCBz)COOH and 4-hydroxyproline. In a fibrin clotting assay with human thrombin and bovine fibrinogen, another product (III) showed an IC50 (concentration required to double the clotting time relative to a control) of 47 μM.

L22 ANSWER 26 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:217491 HCAPLUS Full-text
TITLE: Synthesis and structure-activity relationship of heteronaphthoquinone nonglycosides.
AUTHOR(S): **St-Denis, Y.**; Hinnant, E.; Yates, J.; Bixler, J.; Attardo, G.
CORPORATE SOURCE: BioChem Therapeutic Inc., Laval, QC, H7V 4A7, Can.
SOURCE: Book of Abstracts, 211th ACS National Meeting, New Orleans, LA, March 24-28 (1996), CARB-050. American Chemical Society: Washington, D. C.
CODEN: 62PIAJ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB Following our discovery that the structure of the glycosidic portion of numerous heteronaphthoquinones could accommodate a vast variety of modifications, we decided to explore the possibility of replacing the sugar altogether with simple nonglycosidic moieties. Several isosteres such as piperidines and pyrrolidines were envisaged, yielding potent analogs (1). The SAR of (1) with respect to the in vitro antitumor potency and MDR will be presented.

L22 ANSWER 27 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:209652 HCAPLUS Full-text

DOCUMENT NUMBER: 124:261735
TITLE: Preparation of purinylalkoxycarbonylarginines and related compounds as immunostimulants.
INVENTOR(S): Penney, Christopher; Zacharie, Boulos; Gagnon, Lyne; Attardo, Giorgio; Connolly, Timothy; **St-Denis, Yves**; Kadhim, Salam; Ely, Guy
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9535297	A1	19951228	WO 1995-CA356		19950621
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT					
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9526667	A	19960115	AU 1995-26667		19950621
ZA 9505131	A	19970324	ZA 1995-5131		19950621
EP 766683	A1	19970409	EP 1995-921669		19950621
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
CN 1157618	A	19970820	CN 1995-194679		19950621
CN 1051083	B	20000405			
JP 10501533	T	19980210	JP 1995-501429		19950621
HU 77780	A2	19980828	HU 1996-3492		19950621
BR 9508115	A	19981103	BR 1995-8115		19950621
RU 2191189	C2	20021020	RU 1997-100789		19950621
PL 184342	B1	20021031	PL 1995-317902		19950621
NO 9605394	A	19970221	NO 1996-5394		19961213
NO 317552	B1	20041115			
FI 9605040	A	19970221	FI 1996-5040		19961216
PRIORITY APPLN. INFO.:			US 1994-264028	A	19940622
			WO 1995-CA356	W	19950621

OTHER SOURCE(S): MARPAT 124:261735
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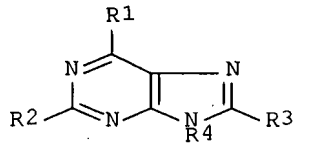

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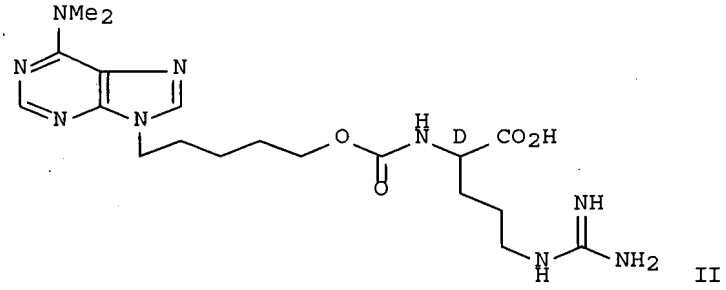

II

AB Title compds. [I; R1 = H, alkyl, halo, (substituted) thiol, amino, OR8; R8 = H, alkyl, acyl, aryl; R2, R3 = H, alkyl, amino, halo, (substituted) thiol; R4 = (heteroatom-interrupted) (CH0-2)0-20X12; X12 = OH, aminoalkyl, amino acid, peptide; with provisos], were prepared Thus, title compound (II), prepared by solution phase couplings starting from 6-chloropurine, showed activation of T cells and in combination with 5-fluorouracil inhibited growth of mouse colon adenocarcinoma.

L22 ANSWER 28 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:878880 HCAPLUS Full-text
DOCUMENT NUMBER: 123:285816
TITLE: Preparation of heteronaphthoquinones and glycosides thereof as antitumor drugs.
INVENTOR(S): Attardo, Giorgio; Wang, Wuyi; Breining, Tibor; Li, Tiechao; **St. Denis, Yves**; Kraus, Jean-Louis
PATENT ASSIGNEE(S): Biochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9512588	A1	19950511	WO 1994-CA210	19940506
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9466727	A	19950523	AU 1994-66727	19940506
PRIORITY APPLN. INFO.:			US 1993-148251 A	19931105
			WO 1994-CA210 W	19940506

OTHER SOURCE(S): MARPAT 123:285816
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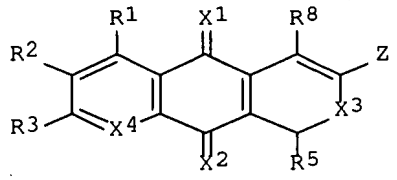

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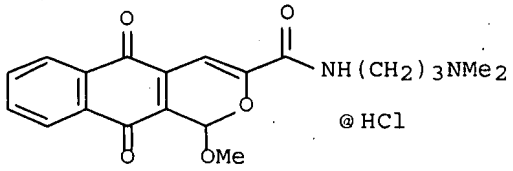

II

AB Title compds. [I; X1, X2 = O, S, NR20; R20 = H, OH, alkyl, acyl, alkylamino; X3 = O, S, SO, SO2, NR21; R21 = OH, acyl, alkyl, aryl, haloacyl, H; X4 = CQ, N, NO; R1-R3, Q = H, OH, alkyl, alkoxy, cycloalkyl, tosyl, mesyl, triflate, thiol, (substituted) acetate, amino, etc.; Z = H, OH, halo, thiol, sulfide, alkoxy, hydroxime, hydrazone, cyano, arylsulfone, alkynyl, squarate, Ph, (substituted) amino, acylamino, heterocyclyl, carboxylate ester, etc.; R5, R8 = H, halo, OH, alkoxy, alkyl, acetylenyl, cycloalkyl, alkenyl, alkoxyalkylamino, cyano, aminoalkyl, acyl, carboxylate ester, acosamine, glucosamine, 2,6-dideoxyrhamnose, thioglucose, thiodaunosamine residue, (substituted) (aromatic) ring, etc.], were prepared Thus, naphthopyran derivative (II) [preparation from Me (5,8-dimethoxyisochroman-3-yl)carboxylate given] showed IC50 = 0.0073-0.029 μM against SKOV3 ovarian carcinoma cells.

L22 ANSWER 29 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:524784 HCAPLUS Full-text
DOCUMENT NUMBER: 123:112575
TITLE: Synthesis of analogs of daunosamine
AUTHOR(S): **St. Denis, Yves**; Lavallee, Jean-Francois; Nguyen, Dieu; Attardo, Giorgio
CORPORATE SOURCE: BioChem Therapeutique, Laval, Quebec, H7V 1B7, Can.
SOURCE: Synlett (1995), (3), 272-4
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Thieme
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Protected acosamine, 2,3,4,6-tetradeoxy-3-amino-4-iodo-L-lyxohexopyranose, 2,3,4,6-tetradeoxy-4-amino-L-lyxo-hexopyranose as well as daunosamine were synthesized using a modification of Kolar's methodol.

L22 ANSWER 30 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:323950 HCAPLUS Full-text
DOCUMENT NUMBER: 120:323950
TITLE: Studies toward the synthesis of hydroxylated indolizidine alkaloids
AUTHOR(S): **St. Denis, Yves**
CORPORATE SOURCE: McGill Univ., Montreal, QC, Can.
SOURCE: (1991) 228 pp. Avail.: NLC, Order No. DANN74913

From: Diss. Abstr. Int. B 1993, 54(1), 253
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L22 ANSWER 31 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:255856 HCAPLUS Full-text
DOCUMENT NUMBER: 116:255856
TITLE: Synthesis of 1-deoxycastanospermine and stereoisomers
AUTHOR(S): **St. Denis, Yves**; Chan, Tak Hang
CORPORATE SOURCE: Dep. Chem., McGill Univ., Montreal, QC, H3A 2K6, Can.
SOURCE: Journal of Organic Chemistry (1992), 57(11), 3078-85
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 116:255856
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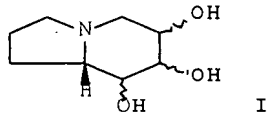

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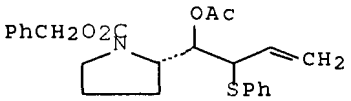

II

AB Four different isomers of 1-deoxycastanospermine (6,7,8-trihydroxyindolizidine) (I) were synthesized. Their basic skeleton was constructed from a proline derivative and the anion of allyl Ph sulfide, followed by an allylic sulfide rearrangement of pyrrolidine derivative II and a subsequent nucleophilic cyclization. The aminotriols were obtained in good yields with a concise overall sequence.

L22 ANSWER 32 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:67214 HCAPLUS Full-text
DOCUMENT NUMBER: 106:67214
TITLE: Synthetic utility of chiral tetrahydrofurans: preparation of (1R,3R,5S)-1,3-dimethyl-2,9-dioxabicyclo[3.3.1]nonane
AUTHOR(S): Guindon, Yvan; **St. Denis, Yves**; Daigneault, Sylvain; Morton, Howard E.
CORPORATE SOURCE: Merck Frosst Canada Inc., Pointe Claire-Dorval, QC, H9R 4P8, Can.
SOURCE: Tetrahedron Letters (1986), 27(11), 1237-40
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 106:67214
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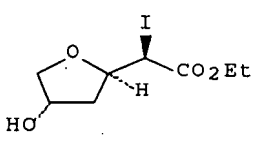

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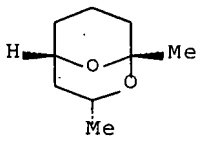

II

AB The use of the iodoetherification reaction for the selective preparation of optically active trans-2,4-disubstituted tetrahydrofurans e.g. I and the use of the latter compds. as precursors of syn-1,3-diols is exemplified in the synthesis of the title compound II.

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